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U.S. Patent No. 4278689
Issued July 14, 1981

#16

Inventors: Keith C. Murdock
Frederick E. Durr

Assignee: AMERICAN CYANAMID COMPANY, One Cyanamid Plaza, Wayne, New Jersey 07470

Title: 1,4-Bis(Substituted-Amino)-5,8-Dihydroxy-anthraquinones and Leuco Bases Thereof

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

SIR:

APPLICATION FOR EXTENSION
OF PATENT TERM

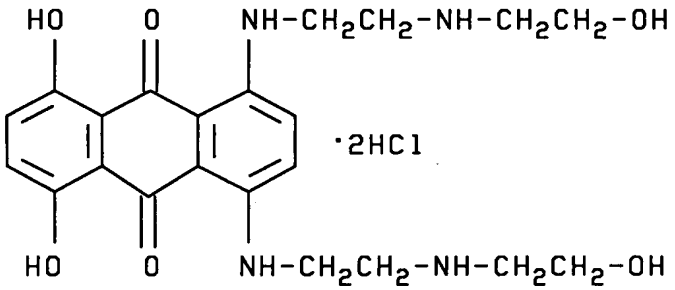
This application, filed in duplicate, is respectfully submitted pursuant to the provisions of 35 U.S. Code 156, Extension of Patent Term. It is hereby certified that the duplicate application is identical to this original application. An extension of the term of U.S. Patent No. 4278689 claiming compositions containing the "approved product" (as defined hereinafter) is respectfully requested.

Applicant has determined and submits that U.S. Patent No. 4278689 is subject to, and meets the conditions for, extension of its term in compliance with the GUIDELINES FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156, published in 1047 OG 16-20 (1984), section A paragraphs (a)-(b) and section B paragraphs (a)-(g) thereof, and that this application for extension of patent term is being submitted in compliance with section C thereof.

P 30042 02/18/88 4278689 01-1300 030 111 550.00CH

The following paragraph numbers correspond to those in the GUIDELINES FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156, section D paragraph (b) thereof:

(1) The approved product is 1,4-bis[2-(2-hydroxy-ethylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride which may be represented by the following structural formula:



in association with a pharmaceutical carrier. The approved product is an antineoplastic agent which is marketed abroad under the generic name mitoxantrone hydrochloride and the trade name Novantrone®.

(2) The Federal statute under which the regulatory review occurred is the Federal Food, Drug, and Cosmetic Act (June 25, 1938, ch. 675, §505, 52 Stat. 1052).

(3) The approved product, identified in paragraph (1) above, received permission for commercial marketing on December 23, 1987.

(4) This application is being submitted within the sixty day period permitted for submission under 35 U.S.C. 156. The last day on which the application could be submitted is February 20, 1988.

(5) The patent for which an extension is being sought is U.S. Patent No. 4278689, issued July 14, 1981 to inventors Keith C. Murdock and Frederick E. Durr.

(6) A copy of the patent for which an extension is being sought, in single column form, is attached to this application and is identified as Exhibit A.

(7) A copy of the only certificate of correction filed in U.S. Patent No. 4278689 is attached to this application and is identified as Exhibit B. No disclaimer has been filed in this patent. No maintenance fees are due on this patent since it is based on an application filed prior to December 12, 1980 (37 CFR 1.20). No reexamination certificate has issued in this patent. The assignee of record has not filed a request for reexamination and has no knowledge of any third party filing such a request.

(8) Claims 1, 3, 12 and 18 of U.S. Patent No. 4278689 claim pharmaceutical compositions wherein the approved product is either specifically or generically recited as the active ingredient therein. The approved product is within the scope of the definition of the active ingredient in Claims 1, 3 and 18 whereas Claim 12 specifically recites the approved product as the active ingredient.

(9) The relevant dates and information pursuant to 35 U.S.C. 156(g) are:

April 16, 1979 - effective date of investigational exemption for a new drug under §505(i)-hereafter IND No. 16-332.

May 18, 1984 - effective date of new drug application under §505(b)-hereafter NDA No. 19-297.

Dec. 23, 1987 - effective date of approval of NDA No. 19-297.

(10) A brief description of the activities undertaken by the assignee of record of U.S. Patent No. 4278689 during the regulatory review period with

respect to the approved product is attached to this application and is identified as Exhibit C.

(11) In the opinion of the applicant, U.S. Patent No. 4278689 is eligible for an extension of its term of two years. The length of extension was determined as follows:

(a) The period of IND No. 16-332; which is the period beginning on the issue date of the patent and ending on the filing date of NDA No. 19-297 which is from July 14,1981 to May 18,1984; is 1,040 days.

(b) The period of NDA No. 19-297; which is the period beginning on the date the application was initially submitted and ending on the date such application was approved which is from May 18,1984 to December 23,1987; is 1,315 days.

(c) Pursuant to 35 U.S.C. 156(c), the period of extension equals one-half the period of IND No. 16-332 plus the period of NDA No. 19-297 which is 1,040/2 + 1,315 which is 1,835 days.

(d) <u>HOWEVER:</u> U.S. Patent No. 4278689 issued before the date of enactment of 35 U.S.C. 156, and a request for an exemption described in 35 U.S.C. 156(g)(1)(B) with respect to the approved product was submitted before such date of enactment, and the commercial marketing or use of the product had not been approved before such date of enactment. Therefore, the period of extension pursuant to 35 U.S.C. 156(g)(4)(C) may not exceed two years.

(12) Applicant acknowledges a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to any determinations to be made relative to this application for extension of patent term. Inquiries for such information may be

directed to Messrs. R.P. Raymond (203)348-7331 (Ext. 2672) or E.A. Conroy (203)348-7331 (Ext. 2249).

(13) The Commissioner is hereby authorized to charge Applicant's Deposit Account No. 01-1300 for the prescribed fees for receiving and acting upon this application for extension of patent term and the declaration submitted therewith.

The declaration pursuant to section D paragraph (c) of the GUIDELINES FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156 is attached to this application and is identified as Exhibit D.

It is then respectfully submitted that this application is complete and in order and that U.S. Patent No. 4278689 is entitled to an extension of its term of two years and such action is earnestly solicited.

Alphonse R. Noë, Manager
Patent Law Department
AMERICAN CYANAMID COMPANY
1937 West Main Street
P.O. Box 60
Stamford, CT 06904-0060

February 16, 1988

EAC/jhr
27962A

EXHIBIT A

United States Patent [19]

Murdock et al.

[54] **1,4-BIS(SUBSTITUTED-AMINO)-5,8-DIHYDROXY-ANTHRAQUINONES AND LEUCO BASES THEREOF**

[75] Inventors: **Keith C. Murdock, Pearl River, N.Y.; Frederick E. Durr, Ridgewood, N.J.**

[73] Assignee: **American Cyanamid Company, Stamford, Conn.**

[21] Appl. No.: **63,285**

[22] Filed: **Aug. 2, 1979**

Related U.S. Application Data

[60] Division of Ser. No. 923,602, Jul. 11, 1978, Pat. No. 4,197,249, which is a continuation-in-part of Ser. No. 873,040, Jan. 30, 1978, abandoned, which is a continuation-in-part of Ser. No. 824,872, Aug. 15, 1977, abandoned.

[51] Int. Cl.³ A61K 31/135

[11] **4,278,689**

[45] **Jul. 14, 1981**

[52] U.S. Cl. 424/330

[58] Field of Search 424/330

[56] **References Cited**

U.S. PATENT DOCUMENTS

3,646,072 2/1972 Shaw 260/380

OTHER PUBLICATIONS

Chemical Abstracts 88:83369t (1978).

Primary Examiner—Jerome D. Goldberg
Attorney, Agent, or Firm—Edward A. Conroy, Jr.

[57] **ABSTRACT**

This disclosure describes symmetrical 1,4-bis(substituted-amino)-5,8-dihydroxyanthraquinones useful as chelating agents and for inhibiting the growth of transplanted mouse tumors.

29 Claims, No Drawings

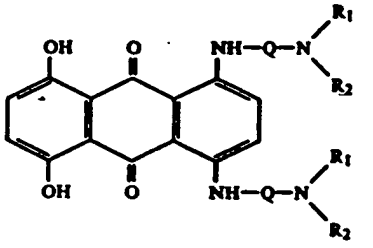
1,4-BIS(SUBSTITUTED-AMINO)-5,8-DIHYDROXY-ANTHRAQUINONES AND LEUCO BASES THEREOF

CROSS REFERENCE TO RELATED APPLICATION

This application is a division of application Ser. No. 923,602, filed July 11, 1978, now U.S. Pat. No. 4,197,249 which is a continuation-in-part of our copending application Ser. No. 873,040, filed Jan. 30, 1978 now abandoned, which is a continuation-in-part of our abandoned application Ser. No. 824,872, filed Aug. 15, 1977.

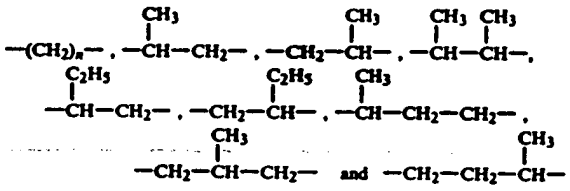
BRIEF SUMMARY OF THE INVENTION

This invention relates to new organic compounds and, more particularly, is concerned with novel symmetrical 1,4-bis(substituted-amino)-5,8-dihydroxyanthraquinones which may be represented by the following general formula:

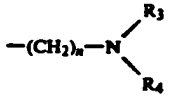


(I)

wherein Q is a divalent moiety selected from the group consisting of those of the formulae:



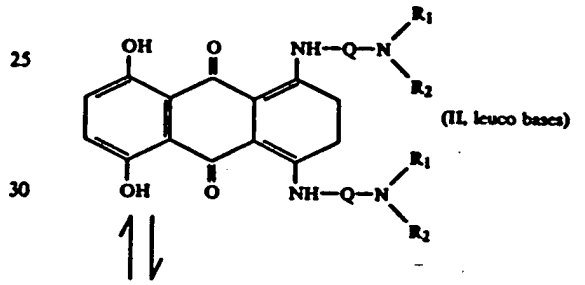
wherein n is an integer from 2 to 4, inclusive: R_1 and R_2 are each individually selected from the group consisting of hydrogen, alkyl from 1 to 4 carbon atoms, monohydroxyalkyl having from 2 to 4 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group, dihydroxyalkyl having from 3 to 6 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group, formyl, alkanoyl having from 2 to 4 carbon atoms, trifluoroacetyl and moieties of the formulae: $—(CH_2)_n—CN$, $—(CH_2)_n—O—R$ and



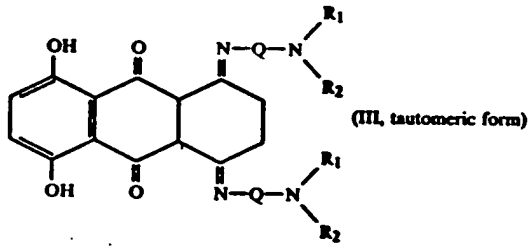
wherein n is an integer from 2 to 4, inclusive, R is alkyl having from 1 to 4 carbon atoms, and R_3 and R_4 are each individually selected from the group consisting of hydrogen, alkyl having from 1 to 4 carbon atoms, and monohydroxyalkyl having from 2 to 4 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group, and R_3 and R_4 taken together with their associated N(itrogen) is morpholino,

chiomorpholino, piperazino, 4-methyl-1-piperazino or a moiety of the formula:

wherein m is an integer from 2 to 6, inclusive; with the first proviso that the ratio of the total number of carbon atoms to the sum of the total number of oxygen atoms plus the total number of nitrogen atoms in the side chains at the 1-position and the 4-position may not exceed 4 and with the second proviso that R_1 and R_2 may not both be hydrogen or alkyl. Suitable monohydroxyalkyl and dihydroxyalkyl groups contemplated by the present invention are, for example, β-hydroxyethyl, β-hydroxypropyl, γ-hydroxypropyl, 2,3-dihydroxypropyl, 2,4-dihydroxybutyl, and the like. Also included within the purview of the present invention are the leuco bases and tautomers thereof which may be represented by the following general formulae:



(II, leuco bases)



(III, tautomeric form)

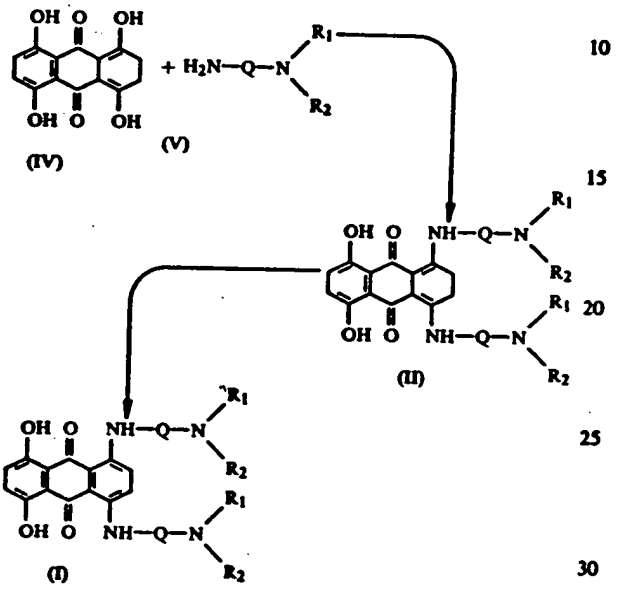
wherein R_1, R_2 and Q are as hereinabove defined.

DETAILED DESCRIPTION OF THE INVENTION

The novel compounds of the present invention are obtainable as reddish brown to blue black crystalline materials having characteristic melting points and absorption spectra and which may be purified by leaching with lower alkanols since many of the free bases are insoluble in water and some of them are insoluble in most organic solvents. The organic bases of this invention (I, II and III) form non-toxic acid-addition salts with a variety of pharmacologically acceptable organic and inorganic salt-forming reagents. Thus, acid-addition salts, formed by admixture of the organic free base with 1,2 or up to eight equivalents of an acid, suitably in a neutral solvent, are formed with such acids as sulfuric, phosphoric, hydrochloric, hydrobromic, sulfamic, citric, lactic, malic, succinic, tartaric, acetic, benzoic, gluconic, ascorbic, and the like. For purposes of this invention the free bases are equivalent to their non-toxic acid-addition salts. The acid-addition salts of the organic bases of the present invention are, in general,

crystalline solids, relatively soluble in water, methanol and ethanol but relatively insoluble in non-polar organic solvents such as diethyl ether, benzene, toluene, and the like.

The novel compounds of the present invention may be readily prepared in accordance with the following reaction scheme:



wherein R_1, R_2 and Q are as hereinabove defined. In accordance with this reaction scheme, leuco 1,4,5,8-tetrahydroxyanthraquinone (IV) is condensed with an appropriate alkylene diamine (V) in a solvent such as N,N,N',N''-tetremethylethylenediamine, methanol, ethanol, water, dimethylformamide, or mixtures thereof at from about 40° C. to about 60° C. under an atmosphere of nitrogen for several hours to produce the corresponding leuco bases (III). The leuco bases (II) may be readily oxidized to the fully aromatic derivatives (I) by a variety of methods such as air oxidation or treatment

with hot nitrobenzene, or treatment with chloranil, hydrogen peroxide, or sodium perborate.

The novel compounds described herein are useful as chelating, complexing or sequestering agents. The complexes formed with polyvalent metal ions are particularly stable and usually soluble in various organic solvents. These properties, of course, render them useful for a variety of purposes wherein metal ion contamination presents a problem; e.g., as stabilizers in various organic systems such as saturated and unsaturated lubricating oils and hydrocarbons, fatty acids and waxes, wherein transition metal ion contamination accelerates oxidative deterioration and color formation. They are further useful in analyses of polyvalent metal ions which may be complexed or extracted by these materials and as metal carriers. Other uses common to sequestering agents are also apparent for these compounds. In addition, the leuco bases (II) are useful as intermediate in the preparation of the fully aromatic derivatives (I).

The novel compounds of the present invention also possess the property of inhibiting the growth of transplanted mouse tumors as established by the following tests.

Lymphocytic leukemia P388 test

The animals used are DBA/2 mice all of one sex, weighing a minimum of 17 g. and all within a 3 gram. weight range. There are 5 or 6 animals per test group. The tumor transplant is by intraperitoneal injection of 0.1 ml. of dilute ascitic fluid containing 10^6 cell of lymphocytic leukemia P388. The test compounds are administered intraperitoneally on days one, 5 and 9 (relative to tumor inoculation) at various doses. The animals are weighed and survivors are recorded on a regular basis for 30 days. The median survival time and the ratio of survival time for treated (T)/control (C) animals are calculated. The positive control compound is 5-fluorouracil given as a 60-mg./kg. injection. The results of this test with representative compounds of the present invention appear in Table I. The criterion for efficacy is $T/C \times 100 \geqq 125\%$.

TABLE I

	Lymphocytic Leukemia P388 Test		
Compound	Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
Leuco-1,4-bis[(2-dimethylamino-ethyl)amino]-5,8-dihydroxy-anthraquinone	100	24.5	245
	50	24.5	245
	25	19.0	190
	12	17.5	175
	6	16.0	160
	3	14.5	145
	1.5	13.0	130
Control	0	10.0	—
5-Fluorouracil	60	19.0	190
1,4-Bis[(2-dimethylaminoethyl)-amino]-5,8-dihydroxy-anthraquinone	50	25.0	278
	25	20.5	228
	12	23.0	256
	6	21.0	233
	3	19.5	217
Control	0	9.0	—
5-Fluorouracil	60	19.5	217
Leuco-1,4-bis(2-morpholinoethyl-amino)-5,8-dihydroxy-anthraquinone	200	13.0	137
	100	12.0	126
	50	11.0	116
	25	12.0	126
Control	0	9.5	—
5-Fluorouracil	60	19.5	205
1,4-Bis(2-morpholinoethylamino)-5,8-dihydroxy-anthraquinone	200	14.0	147
	100	12.0	126
Control	0	9.5	—
5-Fluorouracil	60	19.5	205

TABLE I-continued

Compound	Lymphocytic Leukemia P388 Test Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
Leuco-1,4-bis[(2-diethylamino-ethyl)amino]-5,8-dihydroxy-anthra-quinone	200	17.0	179
	100	17.0	179
	50	15.0	158
	25	13.0	137
	12	12.0	126
Control	0	9.5	—
5-Fluorouracil	60	19.5	205
1,4-Bis[(2-diethylaminoethyl)-amino]-5,8-dihydroxy-anthraquinone	200	20.0	210
	100	18.0	189
	50	15.0	158
	25	16.0	168
	12	12.0	126
Control	0	9.5	—
5-Fluorouracil	60	19.5	205
Leuco-1,4-bis[[2-(1-pyrrolidinyl)-ethyl]amino]-5,8-dihydroxy-anthra-quinone	200	23.0	209
	100	19.0	173
	50	16.0	145
	25	15.0	136
Control	0	11.0	—
5-Fluorouracil	60	20.0	182
1,4-Bis[[2-(1-pyrrolidinyl)ethyl]-amino]-5,8-dihydroxy-anthraquinone	100	24.0	218
	50	23.0	209
	25	21.0	191
	12	18.0	164
Control	0	11.0	—
5-Fluorouracil	60	20.0	182
1,4-Bis[(3-dimethylaminopropyl)-amino]-5,8-dihydroxy-anthraquinone	50	15.5	129
	25	15.5	129
	12	15.0	125
Control	0	12.0	—
5-Fluorouracil	60	19.5	162
Leuco-1,4-bis[(2-aminoethyl)-amino]-5,8-dihydroxy-anthraquinone	100	19.0	158
	50	23.0	192
	25	19.0	158
	12	18.0	150
Control	0	12.0	—
6-Fluorouracil	60	19.5	162
Leuco-1,4-bis(3-aminopropylamino)-5,8-dihydroxy-anthraquinone	200	18.0	150
	100	18.0	150
	50	16.0	133
	25	18.0	150
	12	16.0	133
Control	0	12.0	—
5-Fluorouracil	60	19.5	162
Leuco-1,4-bis[2-(2-methylamino-ethylamino)ethylamino]-5,8-dihy-droxyanthraquinone	200	2.0	18.0
	100	26.0	236.0
	50	28.0	255.0
	1	21.0	191.0
	12.5	16.0	145.0
	6.2	15.0	136
Control	0	11.0	—
5-Fluorouracil	60	17.0	170
Leuco-1,4-bis[2-dimethylaminopro-pylamino]-5,8-dihydroxyanthraqui-none	200	18.0	200
	100	15.0	167
	50	14.0	156
	25	13.0	144
	12.5	11.0	122
Control	0	9.0	—
5-Fluorouracil	60	18.5	206
1,4-Bis[2-(2-hydroxyethylamino) ethylamino]-5,8-dihydroxyanthra-quinone Dihydrochloride	12.5	13.0	130
	6.2	20.0	200
	3.1	22.0	220
	1.5	>29.0	>290
	0.78	>29.0	>290
	0.39	27.0	270
	0.19	25.0	250
	0.09	21.0	210
	0.04	20.0	200
Control	0	10.0	—
5-Fluorouracil	60	20.0	200
1,4-Bis[2-(1-piperazinyl) ethylamino]-5,8-dihydroxyanthra-quinone	200	7.0	78
	100	21.0	233
	50	16.0	178
	25	15.0	167
	12.5	14.0	156
Control	0	9.0	—
5-Fluorouracil	60	18.5	206
1,4-Bis[2-(methylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydro-	25	9.0	86
	12.5	16.0	152

TABLE I-continued

Compound	Lymphocytic Leukemia P388 Test: Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
chloride	6.2	20.0	190
	3.1	22.0	210
	1.5	22.5	214
	0.78	18.5	176
	0.39	19.5	186
	0.19	18.5	176
	0.09	18.0	171
	0.04	17.0	162
Control	0	10.5	—
5-Fluorouracil	60	18.0	171
Leuco-1,4-bis[2-(2-hydroxyethylamino) ethylamino]-5,8-dihydroxyanthraquinone	25	12.0	114
	12.5	23.5	224
	6.2	23.0	219
	3.1	26.0	248
	1.5	>30.0	>286
	0.78	28.0	267
	0.39	22.0	209
	0.19	21.5	205
	0.09	21.5	205
	0.04	18.5	176
Control	0	10.5	—
5-Fluorouracil	60	18.0	171
Leuco-1,4-bis(4-aminobutyl-amino)-5,8-dihydroxyanthra-quinone	400	20.0	190
	300	18.0	171
	200	17.0	162
	100	14.0	133
Control	0	10.5	—
5-Fluorouracil	60	17.5	162
Leuco-1,4-bis[2-(methyl-amino)ethylamino]-5,8-dihydroxyanthraquinone	50	6.0	55
	25	19.0	173
	12.5	19.0	173
	6.2	21.0	191
	3.1	15.0	136
	1.5	13.0	118
Control	0	11.0	—
5-Fluorouracil	60	18.5	168
Leuco-1,4-bis[2-(2-isopropyl-amino)ethylamino]-5,8-dihy-droxyanthraquinone	100	8.0	73
	50	19.0	173
	25	17.0	155
	12.5	15.0	136
Control	0	11.0	—
5-Fluorouracil	60	20.5	186
1,4-Bis[2-(2-aminoethylamino) ethylamino]-5,8-dihydroxyanth-raquinone	200	17.0	162
	100	16.0	152
	50	14.0	133
	25	13.0	124
Control	0	10.5	—
5-Fluorouracil	60	17.0	162
Leuco-1,4-[2-[di(β-hydroxy-ethyl)amino]ethylamino-5,8-dihydroxyanthraquinone	200	19.0	190
	100	17.0	170
	50	16.0	160
	25	15.0	150
	12.5	13.5	135
	6.2	12.0	120
Control	0	10.0	—
5-Fluorouracil	40	18.0	180
5,8-Bis[2-(2-hydroxy-1-pro-pylamino)ethylamino]1,4-di-hydroxyanthraquinone dihy-drochloride	25	12.0	120
	12.5	24.0	240
	6.2	23.0	230
	3.1	22.0	220
	1.56	19.0	190
	0.78	19.0	190
	0.39	17.5	175
Control	0	10.0	—
5-Fluorouracil	40	18.0	180
1,4-Bis[2,[2-(1-morpholino)ethyl-amino]ethylamino]5,8-dihydroxyan-thraquinone tetrahydrochloride	200	9.5	95
	100	20.0	200
	50	18.5	185
	25	19.5	195
	12.5	15.0	150
	6.2	14.0	140
	3.1	13.0	130
Control	0	10.0	—
5-Fluorouracil	40	18.0	180
1,4-Bis[2-(3-hydroxy-1-propyl-amino)ethylamino]5,8-dihydroxy-anthraquinone dihydrochloride	25	8.5	77
	12.5	>30.0	>273
	6.25	26.0	236
	3.1	25.0	227
	1.56	22.0	200

TABLE I-continued

Compound	Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
	Lymphocytic Leukemia P388 Test		
	0.78	21.5	195
Control	0	11.0	—
5-Fluorouracil	40	18.0	164
Leuco-1,4-bis[2-(3-hydroxy-1-propylamino)ethylamino]5,8-dihydroxyanthraquinone	200	14.0	127
	100	38.0	345
	50	34.0	309
	25	22.0	200
	12.5	19.5	177
	6.25	16.5	150
	3.1	18.5	168
	1.56	19.5	177
	0.78	18.0	164
Control	0	11.0	—
5-Fluorouracil	40	17.0	155
1,4-Bis[2-[di(β-hydroxyethyl)-amino]ethylamino]5,8-dihydroxyanthraquinone dihydrochloride	200	>30.0	>333
	100	22.0	244
	50	20.5	228
	25	21.5	239
	12.5	18.5	206
	6.2	18.5	206
	3.1	19.0	211
	1.56	16.0	178
	0.78	14.5	161
Control	0	9.0	—
5-Fluorouracil	60	20.5	228
Leuco-1,4-bis[3-(2-hydroxy-ethylamino)-1-propylamino]-5,8-dihydroxyanthraquinone	200	33.5	305
	100	27.5	250
	50	25.0	227
	25	18.5	168
	12.5	19.0	173
	6.25	18.0	164
	3.12	15.0	136
Control	0	11.0	—
5-Fluorouracil	40	17.5	159
Leuco-1,4-bis[2-(2-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone	200	9.0	82
	100	26.5	241
	50	24.0	218
	25	20.5	186
	12.5	21.5	195
	6.25	20.0	182
Control	0	11.0	—
5-Fluorouracil	40	17.5	159
1,4-Bis[3-(2-hydroxyethyl-amino)-1-propylamino]5,8-dihydroxyanthraquinone dihydrochloride	100	12.5	114
	50	32.0	291
	25	26.5	241
	12.5	22.5	205
	6.25	19.0	173
	3.12	19.0	173
	1.56	16.0	145
	0.78	15.0	136
Control	0	11.0	—
5-Fluorouracil	40	17.5	159
1,4-Bis[2-(1-aziridino)ethyl-amino]-5,8-dihydroxyanthraquinone	100	28.5	285
	50	21.5	215
	25	20.0	200
	12.5	20.5	205
	6.25	18.5	185
	3.12	19.5	195
	1.56	17.0	170
	0.78	14.0	140
Control	0		—
5-Fluorouracil	60	20.5	205
1,4-Bis[2-(2-methylaminoethyl-amino)ethylamino]-5,8-dihydroxyanthraquinone tetrahydrochloride	100	22.0	220
	50	22.0	220
	25	19.5	195
	12.5	17.0	170
	6.25	16.0	160
	1.12	13.5	135
	1.56	13.0	130
Control	0	10.0	—
5-Fluorouracil	40	16.0	160
1,4-Bis(2-aminoethylamino)-5,8-dihydroxyanthraquinone dihydrochloride	12.5	8.0	73
	6.2	15.5	141
	3.1	30.0	273
	1.56	20.0	182
	0.78	24.5	223
	0.39	25.5	232
	0.19	23.0	209
Control	0	11.0	—

TABLE I-continued

Compound	Lymphocytic Leukemia P388 Test: Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
5-Fluorouracil	60	20.5	186

Lymphocytic leukemia P388 test

The procedure used is the same as for the previously described test for lymphocytic leukemia P388 except that the test compounds are administered orally at various doses rather than intraperitoneally. The results of this test with typical compounds of the present invention appear in Table II. The criterion for efficacy is $T/C \times 100 \geqq 125\%$.

TABLE II

Compound	Lymphocytic Leukemia P388 Test (Oral Drug Administration): Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
Leuco-1,4-bis[(2-dimethylamino-ethyl)amino]-5,8-dihydroxy-anthraquinone	50	16.0	160
	25	13.5	135
	12	12.5	125
Control	0	10.0	—
5-Fluorouracil*	60	19.0	190
1,4-Bis[(2-dimethylaminoethyl)-amino-5,8-dihydroxy-anthraquinone	12	16.0	139
	6	16.0	139
	3	15.0	130
Control	0	11.5	—
5-Fluorouracil*	60	20.0	174

*5-Fluorouracil administered intraperitoneally.

Melanotic Melanoma B16

The animals used are C57BC/6 mice, all of the same sex, weighing a minimum of 17 g. and all within a 3-g. weight range. There are normally 10 animals per test group. A one-gram portion of melanotic melanoma B16

tumor is homogenized in 10 ml. of cold balanced salt solution and a 0.5-ml. aliquot of the homogenate is implanted intraperitoneally into each of the test mice. The test compounds are administered intraperitoneally on days one through 9 (relative to tumor inoculation) at various doses. The animals are weighed and survivors are recorded on a regular basis for 60 days. The median survival time and the ratio of survival time for treated (T)/control (C) animals are calculated. The positive control compound is 5-fluorouracil given as a 20-mg./kg. injection. The results of this test with representative compounds of the present invention appear in Table III. The criterion for efficacy is $T/C \times 100 \geqq 125\%$.

TABLE III

Melanotic Melanoma B16 Test			
Compound	Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
Leuco-1,4-bis[(2-dimethylamino-ethyl)amino]-5,8-dihydroxy-anthra-quinone	25	25.0	151
	12	23.0	139
	6	21.5	130
	3	21.0	127
Control	0	16.5	—
5-Fluorouracil	20	25.0	151
1,4-Bis[(2-dimethylaminoethyl)-amino]-5,8-dihydroxy-anthraquinone	25	24.5	136
	12	28.5	158
	6	27.0	150
	3	25.5	142
Control	0	18.0	—
5-Fluorouracil	20	26.0	144
Leuco-1,4-bis[(2-diethylamino-ethyl)amino]-5,8-dihydroxy-anthra-quinone	50	23.0	139
Control	0	16.5	—
5-Fluorouracil	20	25.0	151
1,4-Bis[(2-diethylaminoethyl)-amino]-5,8-dihydroxy-anthraquinone	50	20.5	125
Control	0	16.5	—
5-Fluorouracil	20	25.0	151
Leuco-1,4-bis[[2-(1-pyrrolidinyl)-ethyl]amino]-5,8-dihydroxy-anthra-quinone	50	23.0	144
	25	22.0	137
	12	21.0	131
Control	0	16.0	—
5-Fluorouracil	20	26.5	166
1,4-Bis[[2-(1-pyrrolidinyl)ethyl]-amino]-5,8-dihydroxy-anthraquinone	25	24.5	153
	12	22.0	137
	6	22.0	137
Control	0	16.0	—
5-Fluorouracil	20	26.5	166
1,4-Bis[(3-dimethylaminopropyl)-amino]-5,8-dihydroxy-anthraquinone	25	20.0	125

TABLE III-continued

Compound	Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
	Melanotic Melanoma B16 Test		
Control	0	16.0	—
5-Fluorouracil	20	26.5	166
Leuco-1,4-bis[(2-aminoethyl)-amino]-5,8-dihydroxy-anthraquinone	12	32.0	200
Control	0	16.0	—
5-Fluorouracil	20	26.5	166
Leuco-1,4-bis(3-aminopropylamino)-5,8-dihydroxy-anthraquinone	50	31.5	197
	25	27.0	169
	12	23.5	147
	6	22.5	141
Control	0	16.0	—
5-Fluorouracil	20	26.5	166
Leuco-1,4-bis[2-(2-methylamino-ethylamino]-5,8-dihydroxyanthra-quinone	50	12.5	73
	25	35.0	206
	12.5	39.5	232
	6.2	28.5	168
Control	0	17.0	—
5-Fluorouracil	20	30.0	176
1,4-Bis[2-(1-piperazinyl) ethylamino]-5,8-dihydroxyanthra-quinone	50	34.5	203
	25	30.5	179
	12.5	26.0	153
	6	22.0	129
	3	20.5	121
Control	0	17.0	—
5-Fluorouracil	20.0	30	176
1,4-Bis[2-(2-aminoethylamino) ethylamino]-5,8-dihydroxyanthra-quinone	50	24.0	150
	25	22.5	141
	12	22.0	138
	6	20.0	125
Control	0	16.0	—
5-Fluorouracil	20	27.0	169
Leuco-1,4-bis[2-dimethylamino-propylamino]-5,8-dihydroxyanthra-quinone	100	21.0	124
	50	28.5	168
	25	24.5	144
	12.5	20.5	121
	6	19.5	115
Control	0	17.0	—
5-Fluorouracil	20	30.0	176
1,4-Bis[2-(2-hydroxyethylamino) ethylamino]-5,8-dihydroxyanthra-quinone dihydrochloride	12	11.0	73
	6	15.0	100
	3	>28.5	>190
	1.5	>34.0	>227
	0.7	>34.0	>227
	0.3	34.0	227
Control	0	15.0	—
5-Fluorouracil	60	23.0	153
Leuco-1,4-bis[2-(2-isopropylamino) ethylamino]-5,8-dihydroxyanthra-quinone	50	6.5	39
	25	31.0	188
	12	30.0	182
	6	25.0	151
Control	0	16.5	—
5-Fluorouracil	20	16.5	100
1,4-Bis[2-(methylamino)ethyl-amino]-5,8-dihydroxyanthra-quinone dihydrochloride	12.5	11.5	59
	6.2	26.5	136
	3.1	49.0	251
	1.5	33.0	169
	0.78	35.0	179
	0.39	25.0	128
	0.19	29.5	151
Control	0	19.5	—
5-Fluorouracil	60	25.0	128
Leuco-1,4-bis(4-aminobutyl-amino)-5,8-dihydroxyanthra-quinone	100	21.0	124
	50	20.0	118
	25	18.5	109
	12	16.0	94
Control	0	17.0	—
5-Fluorouracil	20	30.0	176
Leuco-1,4-bis[2-(2-hydroxy-ethylamino(ethylamino]-5,8-dihydroxyanthraquinone	6	9.5	59
	3	20.5	128
	1.5	30.0	187
	0.75	28.5	178
	0.37	22.0	137
Control	0	16.0	—
5-Fluorouracil	20	27.5	172
Leuco-1,4-bis[2-(methylamino) ethylamino]-5,8-dihydroxyanthra-quinone	12	28.0	175
	6	32.5	203
	3	31.0	194
	1.5	36.0	225
	0.7	27.5	172

TABLE III-continued

Compound	Melanotic Melanoma B16 Test Dose mg./kg.	Median Survival Time (Days)	T/C × 100 (Percent)
Control	0	16.0	—
5-Fluorouracil	20	27.5	172

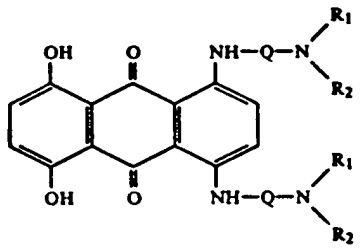
Ridgway Osteogenic Sarcoma

The animals used are AKD_2F_1/J mice, all of the same sex, weighing a minimum of 17 g. and all within a three-gram weight range. There are normally 8 animals per test group. The tumor is administered subcutaneously by trocar as five 2-mm. fragments per mouse. The test compounds are administered intraperitoneally every 4 days for a total of 6 inoculations beginning on day 15 (relative to tumor inoculation) at various doses. The animals are weighed and survivors are recorded on a regular basis for 90 days. The regression of tumors is recorded in all test animals. Table IV gives the result of this test with a representative compound of this invention in terms of the percentage of animals showing tumor regression.

TABLE IV

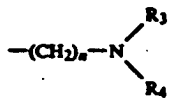
		Ridgway Osteogenic Sarcoma							
		1 Day Before Therapy		7 Days After Therapy Stopped				63 Days After Therapy Stopped	
Compound	Dose (mg./kg.)	No. Mice Per Group	Tumor (mm.)2	No. Without Tumors/No. Survivors	Tumor (mm.)2	% Inhibition Tumor Growth	% Showing 50% Tumor Regression	Median Survival (Days)	T/C (Percent)
Placebo	—	8	64	0/5	1189		0	44.5	
1,4-Bis[(2-di-	100	7	77	2/5	52	96	28	48	108
methylamino-	50	8	68	2/6	263	78	25	92.5	208
ethyl)amino]-	25	8	82	0/8	653	41	0	78	175
5,8-dihydroxy-	12	7	84	0/3	470	61	0	37	83
anthraquinone	6	7	83	0/6	960	19	0	57.5	129
Methotrexate	25	8	51	1/6	546	54	12	52.5	118
	12	8	52	0/9	916	23	0	49	110
	6	8	54	0/4	758	36	0	46	103
Vincristine	1.5	8	42	4/4	0	100	100	68	153
	1.0	6	99	6/6	0	100	100	85	191
	0.5	7	94	4/7	77	93	57	83	186

A preferred embodiment of the present invention may be represented by the following general formula:



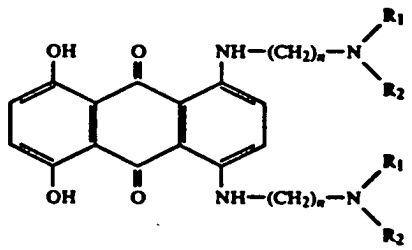
(I)

wherein Q is as hereinbefore defined; R_1 is hydrogen, alkyl having from 1 to 4 carbon atoms or monohydroxyalkyl having from 2 to 4 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group; R_2 is monohydroxyalkyl having from 2 to 4 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group, dihydroxyalkyl having from 3 to 6 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group or a moiety of the formula:



wherein n, R_3 and R_4 are as hereinbefore defined; with the proviso that the ratio of the total number of carbon atoms to the sum of the total number of oxygen atoms plus the total number of nitrogen atoms in each of the side chains at the 1-position and the 4-position may not exceed four. The preferred embodiment includes the corresponding leuco bases of the aromatic bases (I), the tautomers thereof, and the non-toxic pharmaceutically acceptable acid-addition salts thereof.

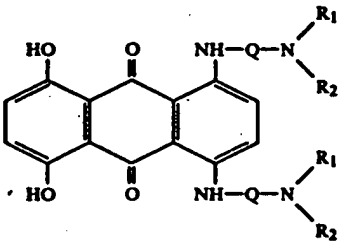
Another preferred embodiment of the present invention may be represented by the following general formula:



(V)

wherein n is an integer from 2 to 4, inclusive, and R_1 and R_2 are as defined for the preceding preferred embodiment with the proviso that the ratio of the total number of carbon atoms to the sum of total number of oxygen atoms plus the total number of nitrogen atoms in each of the side chains at the 1-position and the 4-position may not exceed four. This preferred embodiment also includes the corresponding leuco bases of the aromatic bases (V), the tautomers thereof, and the non-toxic pharmaceutically acceptable acid-addition salts thereof.

Also embraced within the purview of the present invention are therapeutic compositions of matter useful for ameliorating cancer diseases in mammals and containing certain 5,8-dihydroxy-1,4-bis(substituted-amino)anthraquinones (or the leuco bases and non-toxic acid-addition salts thereof) which may be represented by the following structural formula:



(I)

wherein R_1 is hydrogen or alkyl having from 1 to 4 carbon atoms, R_2 is hydrogen or alkyl having from 1 to 4 carbon atoms, R_1 and R_2 taken together with their associated N(itrogen) is as hereinbefore defined for R_3 and R_4 taken together with their associated N(itrogen), and Q is as hereinbefore defined.

The active ingredients of the therapeutic compositions and the novel compounds of the present invention inhibit transplanted mouse tumor growth when administered in amounts ranging from about 5 mg. to about 200 mg. per kilogram of body weight per day. A preferred dosage regimen for optimum results would be from about 5 mg. to about 50 mg. per kilogram of body weight per day, and such dosage units are employed that a total of from about 350 mg. to about 3.5 grams of the active compound for a subject of about 70 kg. of body weight are administered in a 24-hour period. This dosage regimen may be adjusted to provide the optimum therapeutic response. For example, several divided doses may be administered daily or the dose may be proportionally reduced as indicated by the exigencies of the therapeutic situation. A decided practical advantage is that the active compound may be administered in any convenient manner such as by the oral, intravenous, intramuscular, or subcutaneous routes.

The active compounds may be orally administered, for example, with an inert diluent or with an assimilable edible carrier, or they may be enclosed in hard or soft shell gelatin capsules, or they may be compressed into tablets, or they may be incorporated directly with the food of the diet. For oral therapeutic administration, the active compounds may be incorporated with excipients and used in the form of ingestible tablets, buccal tablets, troches, capsules, elixirs, suspensions, syrups, wafers, and the like. Such compositions and preparations should contain at least 0.1% of active compound. The percentage of the compositions and preparations may, of course, be varied and may conveniently be between about 2 to about 60% of the weight of the unit. The amount of active compound in such therapeutically useful compositions is such that a suitable dosage will be obtained. Preferred compositions or preparations according to the present invention are prepared so that an oral dosage unit form contains between about 5 and 200 milligrams of active compound.

The tablets, troches, pills, capsules and the like may also contain the following: A binder such as gum tragacanth, acacia, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as corn starch, potato starch, alginic acid and the like; a

lubricant such as magnesium stearate; and a sweetening agent such as sucrose, lactose or saccharin may be added or a flavoring agent such as peppermint, oil of wintergreen, or cherry flavoring. When the dosage unit form is a capsule, it may contain, in addition to materials of the above type, a liquid carrier. Various other materials may be present as coatings or to otherwise modify the physical form of the dosage unit. For instance, tablets, pills, or capsules may be coated with shellac, sugar or both. A syrup or elixir may contain the active compound, sucrose as a sweetening agent, methyl and propylparabens as preservatives, a dye and flavoring such as cherry or orange flavor. Of course, any material used in preparing any dosage unit form should be pharmaceutically pure and substantially non-toxic in the amounts employed. In addition, the active compounds may be incorporated into sustained-release preparations and formulations.

The active compounds may also be administered parenterally or intraperitoneally. Solutions of the active compound as a free base or pharmacologically acceptable salt can be prepared in water suitably mixed with a surfactant such as hydroxypropylcellulose. Dispersions can also be prepared in glycerol, liquid polyethylene glycols, and mixtures thereof and in oils. Under ordinary conditions of storage and use, these preparations contain a preservative to prevent the growth of microorganisms.

The pharmaceutical forms suitable for injectable use include sterile aqueous solutions or dispersions and sterile powders for the extemporanous preparation of sterile injectable solutions or dispersions. In all cases the form must be sterile and must be fluid to the extent that easy syringability exists. It must be stable under the conditions of manufacture and storage and must be preserved against the contaminating action of microorganisms such as bacteria and fungi. The carrier can be a solvent or dispersion medium containing, for example, water, ethanol, polyol (for example, glycerol, propylene glycol, and liquid polyethylene glycol, and the like), suitable mixtures thereof, and vegetable oils. The proper fluidity can be maintained, for example, by the use of a coating such as lecithin, by the maintenance of the required particle size in the case of dispersion and by the use of surfactants. The prevention of the action of microorganisms can be brought about by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, sorbic acid, thimerosal, and the like. In many cases, it will be preferable to include isotonic agents, for example, sugars or sodium chloride. Prolonged absorption of the injectable compositions can be brought about by the use in the compositions of agents delaying absorption, for example, aluminum monostearate and gelatin.

Sterile injectable solutions are prepared by incorporating the active compound in the required amount in the appropriate solvent with various of the other ingredients enumerated above, as required, followed by filtered sterilization. Generally, dispersions are prepared by incorporating the various sterilized active ingredient into a sterile vehicle which contains the basic dispersion medium and the required other ingredients from those enumerated above. In the case of sterile powders for the preparation of sterile injectable solutions, the preferred methods of preparation are vacuum drying and the freeze-drying technique which yield a powder of the

active ingredient plus any additional desired ingredient from a previously sterile-filtered solution thereof.

As used herein, "pharmaceutically acceptable carrier" includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for pharmaceutical active substances is well known in the art. Except insofar as any conventional media or agent is incompatable with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions.

It is especially advantageous to formulate parenteral compositions in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the mammalian subjects to be treated; each unit containing a predetermined quantity of active material calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier. The specification for the novel dosage unit forms of the invention are dictated by and directly dependent on (a) the unique characteristics of the active material and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active material for the treatment of disease in living subjects having a diseased condition in which bodily health is impaired as herein disclosed in detail.

The principal active ingredient is compounded for convenient and effective administration in effective amounts with a suitable pharmaceutically-acceptable carrier in dosage unit form as hereinbefore disclosed. A unit dosage form can, for example, contain the principal active compound in amounts ranging from about 0.1 to about 400 mg., with from about one to about 30 mg. being preferred. Expressed in proportions, the active compound is generally present in from about 0.1 to about 400 mg./ml. of carrier. In the case of compositions containing supplementary active ingredients, the dosages are determined by reference to the usual dose and manner of administration of the said ingredients.

This invention will be described in greater detail in conjunction with the following specific examples.

EXAMPLE 1

Leuco-1,4-bis[(2-dimethylaminoethyl)amino]-5,8-dihydroxy-anthraquinone

A reaction mixture comprising 10.58 g. of N,N-dimethylethylenediamine, 60 ml. of N,N,N',N'-tetramethylethylenediamine and 10.96 g. of leuco-1,4,5,8-tetrahydroxyanthraquinone is flushed with nitrogen and stirred under nitrogen for 2 hours while heating with an oil bath kept at 49°–51° C. The mixture is allowed to cool under nitrogen. The solid is collected and washed with ethanol giving 14.78 g. of the desired product as a dark red-brown solid.

EXAMPLE 2

1,4-Bis[(2-dimethylaminoethyl)amino]-5,8-dihydroxyanthraquinone

A 12.00-g. portion of leuco-1,4-bis[(2-dimethylaminethyl)amino]-5,8-dihydroxy-anthraquinone in 100 ml. of nitrobenzene is heated under reflux for 15 minutes and then filtered while hot. The filtrate is reheated to boiling, allowed to cool, and the solid is collected and

washed with ethanol giving 8.44 g. of the desired product as blue-black crystals, mp. 236°–238° C.

EXAMPLE 3

Leuco-1,4-bis(2-morpholinoethylamino)-5,8-dihydroxyanthraquinone

A solution of 15.62 g. of N-(2-aminoethyl)morpholine in 40 ml. of N,N,N',N'-tetramethylethylenediamine is de-aerated by bubbling nitrogen through it for 15 minutes. A 10.97-g. portion of leuco-1,4,5,8-tetrahydroxyanthraquinone is added slowly with stirring and the suspension is treated as described in Example 1, giving 18.07 g. of the desired product as an olive solid, mpm 223°–227° C.

EXAMPLE 4

1,4-Bis(2-morpholinoethylamino)-5,8-dihydroxyanthraquinone

A 13.90-g. portion of leuco-1,4-bis(2-morpholinoethylamino)-5,8-dihydroxy-anthraquinone in 100 ml. of nitrobenzene is oxidized as described in Example 2 giving 10.30 g. of the desired product as black rods, mp. 241°–243° C.

EXAMPLE 5

Leuco-1,4-bis[(2-diethylaminoethyl)amino]-5,8-dihydroxyanthraquinone

The procedure of Example 3 is repeated using 13.95 g. of N,N-diethylethylenediamine in place of the N-(2-aminoethyl)morpholine, giving 13.97 g. of the desired product as a red-brown solid, mp. 182°–185° C.

EXAMPLE 6

1,4-Bis[(2-diethylaminoethyl)amino]-5,8-dihydroxyanthraquinone

A 10.90-g. portion of leuco-1,4-bis[(2-diethylaminoethyl)amino]-5,8-dihydroxyanthraquinone is oxidized as described in Example 2 giving 6.35 g. of the desired product as blue-black needles, mp. 202°–204° C.

EXAMPLE 7

Leuco-1,4-bis[2-(1-pyrrolidinyl)ethylamino]-5,8-dihydroxyanthraquinone

The procedure of Example 3 is repeated using 12.05 g. of N-2-pyrrolidinoethylamine, in place of the N-(2-aminoethyl)morpholine, and 80 ml. of N,N,N',N'-tetramethylethylenediamine, giving 13.24 g. of the desired product as a red-brown solid, mp. 180°–185° C.

EXAMPLE 8

1,4-Bis[2-(1-pyrrolidinyl)ethylamino]-5,8-dihydroxyanthraquinone

An 8.61-g. portion of leuco-1,4-bis[[2-(1pyrrolidinyl-)ethyl]amino]-5,8-dihydroxyanthraquinone is oxidized as described in Example 2. The reaction mixture is evaporated to dryness and the residue recrystallized from toluene, giving 5.12 g. of the desired product as blue-black crystals, mp. 193°–196° C.

EXAMPLE 9

Leuco-1,4-bis[2-(methylamino)ethylamino]-5,8-dihydroxyanthraquinone

The procedure of Example 7 is repeated using 8.90 g. of N-methylethylenediamine in place of the N-2-pyr-

rolidinoethylamine, giving 13.73-g. of the desired product as a dark green solid, mp. 157°–160° C.

EXAMPLE 10

Leuco-1,4-bis[(3-dimethylaminopropyl)amino]-5,8-dihydroxyanthraquinone

Nitrogen is bubbled through an 80-ml. portion of dimethylaminopropylamine for 15 minutes. A 10.97-g. portion of leuco-1,4,5,8-tetrahydroanthraquinone is added slowly with stirring. The mixture is heated under nitrogen at 50°–52° C. for 2 hours and then allowed to cool. The solid is collected and washed with cold ethanol giving 5.59-g. of dark, orange-red crystals, mp. 115°–118° C.

EXAMPLE 11

1,4-Bis[(3-dimethylaminopropyl)amino]-5,8-dihydroxyanthraquinone

A suspension of 6.00-g. of leuco-1,4-bis[(3-dimethylaminopropyl)amino]-5,8-dihydroxyanthraquinone in 60 ml. of N,N,N',N'-tetramethylethylenediamine is heated on a steam bath under reflux while air is bubbled in for 12 hours. The solution is cooled, producing a solid which is collected and washed twice with heptane and once with petroleum ether. This solid is recrystallized by extracting with 350 ml. of hot heptane, filtering and concentrating to 300 ml. Crystallization and washing with petroleum ether gives 3.72 g. of the desired product as black needles, mp. 154°–157° C.

EXAMPLE 12

Leuco-1,4-bis(2-aminoethylamino)-5,8-dihydroxyanthraquinone

A reaction mixture comprising 10.97-g. of leuco-1,4,5,8-tetrahydroxyanthraquinone in 80 ml. of de-aerated N,N,N',N'-tetramethylethylenediamine containing 7.22 g. of ethylenediamine is heated and stirred under nitrogen at 48°–50° C. for one hour. The mixture is allowed to stand under a slow flow of nitrogen, producing a solid which is collected and washed with ethyl acetate, acetonitrile and petroleum ether giving 13.8 g. of the desired product as a red-black solid.

EXAMPLE 13

Leuco-1,4-bis(3-aminopropylamino)-5,8-dihydroxyanthraquinone

A suspension of 10.97 g. of leuco-1,4,5,8-tetrahydroxyanthraquinone in a de-aerated solution of 8.90 g. of 1,3-diaminopropane in 80 ml. of N,N,N',N'-tetramethylethylenediamine is stirred and heated at 49° C. for one hour under nitrogen, then allowed to cool. The resulting solid is collected and washed with cold ethanol giving 14.21 g. of the desired product as a black solid.

EXAMPLE 14

Leuco-1,4-bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone

A suspension of 12.5 g. of 2-(2-aminoethylamino)ethanol in 40 ml. of N,N,N',N'-tetramethylethylenediamine is stirred and de-aerated by bubbling nitrogen in for 15 minutes. A 10.97-g. portion of leuco-1,4,5,8-tetrahydroxyanthraquinone is gradually added with stirring. The suspension is heated and stirred under nitrogen in an oil bath at 50°–52° C. for 5 hours. The mixture is allowed to stand and cool under nitrogen for 12

hours. The solid is collected by decantation, macerated in ethanol, collected and washed with ethanol giving 15.06 g. of the desired product as a green-gray solid, mp. 129°–131° C.

EXAMPLE 15

Leuco-1,4-bis[2-[di(β-hydroxyethyl)amino]ethylamino]-5,8-dihydroxyanthraquinone

A solution of 17.8 g. of N,N-di(2-hydroxyethyl)ethylenediamine in 100 ml. of methanol is cooled with an ice bath, stirred, and de-aerated by bubbling in nitrogen for 15 minutes. A 10.97-gram portion of leuco-1,4,5,8-tetrahydroxyanthraquinone is gradually added with stirring and continued cooling. The suspension is heated and stirred under nitrogen in an oil bath at 50°–52° C. for one hour and the mixture is then allowed to stand and cool under nitrogen overnight. The solid is collected and washed with ethanol giving 14.8 g. of a red-brown solid, m.p. 165°–168° C.

EXAMPLE 16

1,4-Bis[2-(methylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride

To a suspension of 11.60 g. (0.03 mole) of leuco-1,4-bis[2-(methylamino)ethylamino]-5,8-dihydroxyanthraquinone in 200 ml. of 2-methoxyethanol was added gradually with stirring 15 ml. of 8 N ethanolic hydrogen chloride. The system was chilled with an ice bath and stirred as 7.50 g. (0.0305 mole) of chloranil powder was gradually added. The mixture was stirred overnight at room temperature and diluted with 600 ml. of ether. The solid was collected and washed with tetrahydrofuran. The product (14.16 g.) was recrystallized by dissolving it in 130 ml. of water and adding 650 ml. of acetone to give 13.15 g. of a blue-black solid.

EXAMPLE 17

1,4-Bis[2-(2-aminoethylamino)ethylamino]-5,8-dihydroxyanthraquinone

Following the general procedure of Example 3, a mixture of 10.97-g. of leuco-1,4,5,8-tetrahydroxyanthraquinone, 80 ml. of N,N,N',N'-tetramethylethylenediamine and 21.84-g. (0.24 mole) of diethylenetriamine soon gave a thick, congealed mass which prevented effective stirring so the reaction time was extended to 24 hours. The mixture was allowed to cool and the supernatent liquid was decanted and discarded. A solution of the congealed mass in 100 ml. of methanol was filtered, then allowed to oxidize in the air for four days in a partially covered flask. The gelatinous mass which had separated became solid when the oxidation mixture was agitated with 200 ml. of acetonitrile and then allowed to stand for one hour. After the solid was collected and washed first with acetonitrile, then with ether, it amounted to 10.88 g. of a blue-black powder.

EXAMPLE 18

Leuco-1,4-bis(4-aminobutylamino)-5,8-dihydroxyanthraquinone

Following the general procedure of Example 3 but using 45 ml. of 1,4-diaminobutane as the primary amine component, there was obtained 12.20 g. of product as a dull grey-green solid.

EXAMPLE 19

Leuco-1,4-bis[2-dimethylaminopropylamino]-5,8-dihydroxyanthraquinone

The reaction of 12.26 g. of 2-dimethylaminopropylamine with 10.97 g. of leuco-1,4,5,8-tetrahydroxyanthraquinone in 100 ml. of ethanol for one hour by the procedure of Example 1 gives 7.29 g. of red-brown crystals.

EXAMPLE 20

Leuco-1,4-bis[2-(2-methylaminoethylamino)ethylamino]-5,8-dihydroxyanthraquinone

To a solution of 14.10 g. of 1-methyl diethylenetriamine in 50 ml. of ethanol and 40 ml. of N,N,N',N'-tetramethylethylenediamine is added 10.97 g. of leuco-1,4,5,8-tetrahydroxyanthraquinone as in Example 1. The mixture is heated at 50° and stirred under nitrogen for one hour, chilled with an ice bath, the solid collected and washed with cold ethanol to give 7.23 g. of green-black crystals, m.p. 108°–111° C.

EXAMPLE 21

Leuco-1,4-bis[2-(2-dimethylaminoethylamino)ethylamino]-5,8-dihydroxyanthraquinone

The reaction of N-(dimethylaminoethyl)ethylenediamine with leuco-1,4,5,8-tetrahydroxyanthraquinone by the procedure of Example 20 gives the title compound.

EXAMPLE 22

Leuco-1,4-bis[2-(1-piperazinyl)ethylamino]-5,8-dihydroxyanthraquinone

The procedure of Example 20 applied to 15.50 g. of N-(2-aminoethyl)piperazine gives 3.92 g. of a black powder which does not melt by 350° C. and is discarded. The mother liquor and ethanol washes, on standing and partly evaporating during two weeks in an unstoppered flask, deposit a solid which is collected and washed with ethanol to give 6.19 g. of the title compound as a black solid, m.p. 200°–203° C.

EXAMPLE 23

1,4-Bis(2-aminoethylamino)-5,8-dihydroxyanthraquinone dihydrochloride

Oxidation with chloranil of 28.25 g. of the product of Example 12 by the procedure of Example 16 gives 29.66 g. of a crude, blue-black solid which is then extracted by stirring for 14 hours with 800 ml. of water. Solids are removed by centrifugation and the supernatent solution freeze-dried, leaving 16.38 g. of a blue-black solid which is unmelted by 350° C.

EXAMPLE 24

1,4-Bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone Dihydrochloride

Chloranil oxidation of 17.86 g. of the product of Example 14 by the procedure of Example 16 gives (without recrystallization) 21.34 g. of blue-black solid, m.p. 203°–205° C.

EXAMPLE 25

1,4-Bis[2-(2-methylaminoethylamino)ethylamino]-5,8-dihydroxyanthraquinone Tetrahydrochloride

The product of Example 20 (11.70 g.) is oxidized with chloranil by the procedure of Example 16, giving 18.03 g. of blue-black solid, m.p. 190°–203° C.

EXAMPLE 26

1,4-Bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone

In a modification of the synthesis of Example 14 the solvent used is 100 ml. of ethanol. The mother liquor from the leuco product is allowed to stand for two weeks in an unstoppered flask, whereupon the oxidized product separates. It is collected and washed with ethanol, then recrystallized from ethanol, giving blue-black crystals, m.p. 175°–177° C.

EXAMPLE 27

Leuco-1,4-bis[3-(2-hydroxyethylamino)-1-propylamino]-5,8-dihydroxyanthraquinone

The procedure of Example 15 is used with a solution of 14.18 g. of 2-(3-aminopropylamino)ethanol in 100 ml. of ethanol. The resulting solution is filtered and the filtrate diluted with 300 ml. of ether, precipitating the product as a goo. After decantation of the supernatent solution the goo is caused to crystallize by agitating it with 100 ml. of tetrahydrofuran. Washing with ethanol gives 12.56 g. of green-black solid, m.p. 101°–104° C.

EXAMPLE 28

1,4-Bis[3-(2-hydroxyethylamino)-1-propylamino]-5,8-dihydroxyanthraquinone dihydrochloride

Oxidation of 9.95 g. of leuco-1,4-bis[3-(2-hydroxyethylamino)propylamino]-5,8-dihydroxyanthraquinone with chloranil as in Example 16 gives 11.70 g. of a blue solid which does not melt by 350° C.

EXAMPLE 29

Leuco-1,4-bis[2-(3-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone

The procedure of Example 15 is paralleled with 14.18 g. of N-(3-hydroxypropyl)ethylenediamine in 100 ml. of ethanol to give 14.63 g. of red-brown crystals, m.p. 58°–60° C.

EXAMPLE 30

1,4-Bis[2-(3-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride

Chloranil oxidation of 10.77 g. of the product of Example 29 by the procedure of Example 16 yielded 11.64 g. of a dark blue solid, m.p. 210°–216° C.

EXAMPLE 31

Leuco-1,4-bis[2-(2-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone

With 14.18 g. of 1-(2-aminoethylamino)-2-propanol in 100 ml. of ethanol the procedure of Example 15 yields 17.61 g. of green-black crystals, m.p. 50°–60° C.

EXAMPLE 32

1,4-Bis[2-(2-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride

A filtered solution of 14.44 g. of leuco-1,4-bis[2-(2-hydroxy-1-propylamino)ethylamino]-1,4-dihydroxyanthraquinone in 215 ml. of 2-methoxyethanol is oxidized with 7.65 g. of chloranil by the procedure of Example 16, affording 16.75 g. of purple solid, m.p. 177°–185° C.

EXAMPLE 33

Leuco-1,4-bis[2-[2-(2-hydroxyethylamino)ethylamino]ethylamino]-5,8-dihydroxyanthraquinone

The procedure of example 15 used with a solution of 17.67 g. of 2-[2-(2-aminoethylamino)ethylamino]ethanol in 100 ml. of methanol gives a solution which is filtered, then diluted with 300 ml. of ether, precipitating a goo which hardens on standing overnight. Hardening is completed by thorough maceration of the solid in the solvent. The solid is collected and washed with ether, yielding 16.82 g. of a green-black solid. This solid remains granular if stored at −25° C., but coalesces into a solid cake if stored at 25° C.

EXAMPLE 34

1,4-Bis[2-[2-(2-hydroxyethylamino)ethylamino]ethylamino]-5,8-dihydroxyanthraquinone tetrahydrochloride

Chloranil oxidation of 12.10 g. of the product of Example 33 by the method of Example 16, including three additional washings of the solid with methanol, gives 12.46 g. of dark blue, solid product.

EXAMPLE 35

1,4-Bis[2-(2,3-dihydroxypropylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride

By the procedure of Example 15 a solution of 16.10 g. of 3-(2-aminoethylamino)-1,2-propanediol [A. R. Surrey, C. M. Suter and J. S. Buck, J. Am. Chem. Soc., 74, 4102(1952)] in 100 ml. of methanol gives a goo which is separated from solvent by chilling with an ice bath, then decanting. The goo is washed four times by stirring 1.5 hours at 25° with 100-ml. portions of methanol, chilling with an ice bath, then decanting. A filtered solution of the goo in 280 ml. of 2-methoxyethanol is oxidized with 10.01 g. of chloranil by the method of Example 16. The product is additionally washed with ethanol, giving 15.25 g. of a blue-black solid, m.p. 191°–193° C.

EXAMPLE 36

Leuco-1,4-bis[2-(1-aziridino)ethylamino]-5,8-dihydroxyanthraquinone

With 10.33 g. of N-(2-aminoethyl)aziridine in 80 ml. of N,N,N',N'-tetramethylethylenediamine the procedure of Example 15 gives a stiff gum. The next day the supernatent solution is discarded, 100 ml. of ether is added and the gum periodically macerated therein for another day, when the gum is mostly hardened. Hardening is completed by maceration during three washings of the solid with ether, giving 17.66 g. of blue-black, granular powder.

EXAMPLE 37

1,4-Bis[2-(1-aziridino)ethylamino]-5,8-dihydroxyanthraquinone

To a suspension of 4.10 g. of the product of Example 36 in 40 ml. of chlorodorm is added a solution of 1.74 g. of diethyl azodicarboxylate in 25 ml. of chloroform. The mixture is stirred for 20 minutes, the resulting dark blue solution is filtered, and the filtrate is evaporated at ≦30°. A solution of the residue in 40 ml. of chloroform is stirred five minutes with 2 g. of decolorizing carbon, filtered and washed through with another 25 ml. of chloroform. Addition of 100 ml. of ether to the filtrates precipitates a gum which is eliminated by decantation-filtration. The filtrates deposit crystals which are washed sparingly with acetone. The chloroform-ether mother liquor, chilled at −60° C., deposits a second crop of crystals which is washed with ether and with methanol. A solution of both crops of crystals in 20 ml. of chloroform is stirred with decolorizing carbon, filtered, evaporated at ≦25° C. to a volume of 5 ml., diluted with 20 ml. of ether, then chilled at −60° C. The resulting blue-black crystals, washed with ether, amount to 0.64 g., m.p. 168°–170° C. In thin-layer chromatography on silica gel the product is moved as a blue spot by chloroform-triethylamine-methanol, 27/3/1 (ratios by volume).

EXAMPLE 38

1,4-Bis[2-[2-(1-morpholino)ethylamino]ethylamino]-5,8-dihydroxyanthraquinone tetrahydrochloride

A solution of 20.80 g. of N-(morpholinoethyl)ethylenediamine in 100 ml. of ethanol is used in the procedure of Example 15 to give a solution which is filtered and diluted with 900 ml. of ether, precipitating a goo. The supernatent solution is decanted, the goo dissolved in 175 ml. of 2-methoxyethanol and oxidized with 5.29 g. of chloranil by the method of Example 16, giving 17.7 g. of dark blue solid.

EXAMPLE 39

Leuco-1,4-Bis[2-(acetamido)ethylamino]-5,8-dihydroxyanthraquinone

A solution of 12.26 g. of N-acetylethylene diamine in 100 ml. of ethanol in the procedure of Example 15 gives 15.27 g. of dark, red-brown solid, m.p. 125° C.

EXAMPLE 40

1,4-Bis[2-(acetamido)ethylamino]-5,8-dihydroxyanthraquinone

A suspension of 11.95 g. of leuco-1,4-bis[2-(acetamido)ethylamino]-5,8-dihydroxyanthraquinone is oxidized with 6.76 g. of chloranil during 61 hours by the method of Example 16, giving a very acidic hydrochloride salt which is vonverted to the free base by four washings with water. Crystallization from 110 ml. of dimethyl sulfoxide (boiling only 2 minutes and not attempting a hot filtration), then washing with dimethyl sulfoxide and with ethanol gives 7.76 g. of blue-black solid, m.p. 273°–274° C.

EXAMPLE 41

1,4-Bis[2-[N-(2-hydroxyethyl)triflouroacetamido]ethylamino]-5,8-dihydroxyanthraquinone

A suspension of 1.50 g. of 1,4-bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone in

75 ml. of ethyl triflouroacetate and 75 ml. of methanol is stirred for 10 minutes. Evaporation of the resulting solution in vacuo at 30° C. leaves a residue which is washed and macerated with methylene chloride, giving 2.11 g. of blue-black solid, m.p. 162° C.

EXAMPLE 42

1,4-Bis[2-amino-2-carboxyethylamino]-5,8-dihydroxyanthraquinone.¾ HCl

To a solution of 6.23 g. of dl-α,β-diaminopropionic acid in 30 ml. of warm water is added 1.078 g. of lithium hydroxide and 60 ml. of dimethyl sulfoxide. The system is flushed with nitrogen and 4.12 g. of leuco-1,4,5,8-tetrahydroxyanthraquinone is added gradually with stirring. The mixture is stirred and heated with an oil bath at 50°, first for 15 hours under nitrogen, then for 21 hours as the initial product is oxidized by bubbling in a stream of air. Thin-layer chromatography on silica gel with methanol-water-concentrated ammonia (25/5/1 by volume) shows all the product spots to be blue when the oxidation is complete. After the mixture is cool the solids are removed by filtration and washed once with dimethyl sulfoxide-water (2/1). Addition of 400 ml. of methanol to the filtrates precipitates a solid which is collected and washed with methanol. Further washing with a total of 13. ml. of 0.01 N aqueous acetic acid dissolves virtually all of the solid. Addition of 3 ml. of concentrated hydrochloric acid to the acetic acid filtrates precipitates a blue-black solid which is washed with acetone to give 0.24 g. of the product.

EXAMPLE 43

Leuco-1,4-bis[2-(2-methoxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone

An ethanol solution of N-(2-methoxyethyl)ethylendiamine (U.S. Pat. No. 3,454,640) reacts in the procedure of Example 15 to give the title compound.

EXAMPLE 44

1,4-Bis[2(1,3-oxazolidin-1-yl)ethylamino]-5,8-dihydroxyanthraquinone

A solution of 1.62 g. of 37% aqueous formaldehyde solution in 50 ml. of water is stirred overnight with 4.44 g. of 1,4-bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone. The resulting solid is washed with water to give the product.

EXAMPLE 45

1,4-Bis[2-(tetrahydro-1,3-oxazin-1-yl)ethylamino]-5,8-dihydroxyanthraquinone

A solution of 1.62 ml. of 37% aqueous formaldehyde in 50 ml. of 0.4 N aqueous sodium hydroxide is stirred overnight with 5.45 g. of 1,4-bis[2-(3-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride. The product is obtained by washing the resulting solid with water.

EXAMPLE 46

1,4-Bis[2-(1,3-oxazolidin-2-one-1-yl)ethylamino]-5,8-dihydroxyanthraquinone

A solution of 0.020 g. of sodium in 25 ml. of methanol is stirred and heated under reflux overnight with 75 ml. of diethyl carbonate and 4.44 g. of 1,4-bis[2-(2-hydroxyethylamino)-ethylamino]-5,8-dihydroxyanthraquinone. The mixture is allowed to cool. It is stirred with

0.1 ml. of acetic acid, the solid is collected by filtration and washed with methanol to give the product.

EXAMPLE 47

1,4-Bis[2-(1,3-oxazin-2-one-1-yl)ethylamino]-5,8-dihydroxyanthraquinone

A solution of 0.48 g. of sodium in 25 ml. of methanol is stirred and heated overnight with 75 ml. of diethyl carbonate and 5.45 g. of 1,4-bis[2-(3-hydroxy-1-propylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride. After the mixture cools it is stirred with 0.1 ml. of acetic acid. The solid product is collected by filtration and washed with methanol and then with water.

EXAMPLE 48

1,4-Bis[2-[di(β-hydroxyethyl)amino]ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride

Chloranil oxidation of 10.77 g. of the product of Example 15 by the method of Example 16 gives 11.64 g. of a dark blue solid, m.p. 216° C.

EXAMPLE 49

Preparation of 50 mg. Tablets

Per Tablet		Per 10,000 Tablets
0.050 gm.	1,4-bis(3-aminopropylamino)-5,8-dihydroxyanthraquinone	500 gm.
0.080 gm.	Lactose	800 gm.
0.010 gm.	Corn Starch (for mix)	100 gm.
0.008 gm.	Corn Starch (for paste)	75 gm.
0.148 gm.		1475 gm.
0.002 gm.	Magnesium stearate (1%)	15 gm.
0.150 gm.		1490 gm.

The 1,4-bis(3-aminopropylamino)-5,8-dihydroxyanthraquinone, lactose and corn starch (for mix) are blended together. The corn starch (for paste) is suspended in 600 ml. of water and heated with stirring to form a paste. This paste is then used to granulate the mixed powders. Additional water is used if necessary. The wet granules are passed through a No. 8 hand screen and dried at 120° F. The dry granules are then passed through a No. 16 screen. The mixture is lubricated wth 1% magnesium stearate and compressed into tablets in a suitable tableting machine.

EXAMPLE 50

Preparation of Oral Suspension

Ingredient	Amount
Leuco-1,4-bis(3-aminopropylamino)-5,8-dihydroxyanthraquinone	500 mg.
Sorbitol solution (70% N.F.)	40 ml.
Sodium benzoate	150 mg.
Saccharin	10 mg.
Red dye	50 mg.
Cherry flavor	50 ml.
Distilled water qs. ad.	100 ml.

The sorbitol solution is added to 40 ml. of distilled water and the leuco-1,4-bis(3-aminopropylamino)-5,8-dihydroxyanthraquinone is suspended therein. The saccharin, sodium benzoate, flavor and dye are added and dissolved. The volume is adjusted to 100 ml. with distilled water. Each ml. of syrup contains 5 mg. of leuco-

1,4-bis(3-aminopropylamino)-5,8-dihydroxyanthraquinone.

EXAMPLE 51

Preparation of Parenteral Solution

In a solution of 700 ml. of propylene glycol and 200 ml. of water for injection is suspended 20.0 grams of 1,4-bis[3-(dimethylamino)propylamino]-5,8-dihydroxyanthraquinone dihydrochloride with stirring. After suspension is complete, the pH is adjusted to 5.5 with hydrochloric acid and the volume is made up to 1000 ml. with water for injection. The formulation is sterilized, filled into 5.0 ml. ampoules each containing 2.0 ml. (representing 40 mg. of drug) and sealed under nitrogen.

EXAMPLE 52

1,4-Bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone disuccinate salt

A mixture of 222 mg. of 1,4-bis[2-(2-hydroxyethylamino)-ethylamino]-5,8-dihydroxyanthraquinone, 118 mg. of succinic acid, and 50 ml. of ethanol is heated under reflux for 30 minutes to give the title compound.

EXAMPLE 53

1,4-Bis[2-(3-hydroxypropylamino)ethylamino]-5,8-dihydroxyanthraquinone dimalate salt

A mixture of 228 mg. of 1,4-bis[2-(3-hydroxypropylamino)-ethylamino]-5,8-dihydroxyanthraquinone, 134 mg. of DL-malic acid, and 50 ml. of ethanol is heated under reflux for 30 minutes to give the title compound.

EXAMPLE 54

1,4-Bis[2-(2-hydroxypropylamino)ethylamino]-5,8-dihydroxyanthraquinone dilactate salt

A mixture of 228 mg. of 1,4-bis[2-(2-hydroxypropylamino)-ethylamino]-5,8-dihydroxyanthraquinone, 120 mg. of 80% DL-lactic acid, and 10 ml. of ethanol is heated on a steam bath for 10 minutes, cooled, treated with 50 ml. of acetone and cooled to obtain the title compound.

EXAMPLE 55

Preparation of 50 mg. Tablets

Per Tablet		Per 10,000 Tablets
0.050 gm.	1,4-Bis[2-(2-hydroxyethylamino) ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride	500 gm.
0.080 gm.	Lactose	800 gm.
0.010 gm.	Corn Starch (for mix)	100 gm.
0.008 gm.	Corn Strach (for paste)	75 gm.
0.148 gm.		1475 gm.
0.002 gm.	Magnesium Stearate (1%)	15 gm.
0.150 gm.		1490 gm.

The 1,4-bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride, lactose and corn starch (for mix) are blended together. The corn starch (for paste) is suspended in 600 ml. of water and heated with stirring to form a paste. This paste is then used to granulate the mixed powders. Additional water is used if necessary. The wet granules are passed through a No. 8 hand screen and dried at 120° F. The dry granules are then passed through a No. 16 screen. The mixture is lubricated with 1% magnesium stearate

and compressed into tablets in a suitable tableting machine.

EXAMPLE 56

Preparation of Oral Suspension

Ingredient	Amount
1,4-Bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride	500 mg.
Sorbitol solution (70% N.F.)	40 ml.
Sodium benzoate	150 mg.
Saccharin	10 mg.
Red dye	50 mg.
Cherry flavor	50 ml.
Distilled water qs ad	100 ml.

The sorbitol solution is added to 40 ml. of distilled water and the 1,4-bis[2-(2-hydroxyethylamino)ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride is suspended therein. The saccharin, sodium benzoate, flavor and dye are added and dissolved. The volume is adjusted to 100 ml. with distilled water. Each ml. of syrup contains 5 mg. of 1,4-bis[2-(2-hydroxyethylamino)-ethylamino]-5,8-dihydroxyanthraquinone dihydrochloride.

EXAMPLE 57

1,4-Bis[2-(3-hydroxypropylamino)ethylamino]-5,8-dihydroxyanthraquinone diacetate salt

A mixture of 228 mg. of 1,4-bis[2-(3-hydroxypropylamino)-ethylamino]-5,8-dihydroxyanthraquinone, 60 mg. of glacial acetic acid, and 50 ml. of ethanol is heated under reflux for 30 minutes to give the title compound.

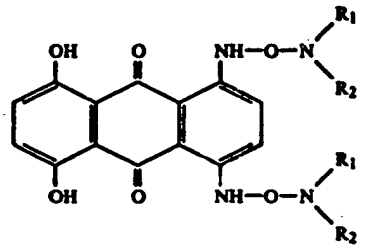
EXAMPLE 58

1,4-Bis[2-(2-hydroxypropylamino)ethylamino]-5,8-dihydroxyanthraquinone diacetate salt

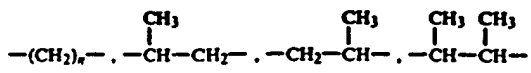
A mixture of 228 mg. of 1,4-bis[2-(2-hydroxypropylamino)-ethylamino]-5,8-dihydroxyanthraquinone, 60 mg. of glacial acetic acid, and 10 ml. of ethanol is heated on a steam bath for 10 minutes, cooled, treated with 50 ml. of acetone and cooled to obtain the title compound.

We claim:

1. A pharmaceutical composition in dosage unit form comprising from about one to about 30 mg. of a compound selected from the group consisting of those of the formula:



wherein Q is a divalent moiety selected from the group consisting of those of the formulae:



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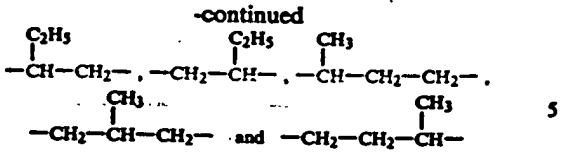


wherein n is an integer from 2 to 4, inclusive; R_1 and R_2 are each individually selected from the group consisting of hydrogen, alkyl having from 1 to 4 carbon atoms and monohydroxyalkyl having from 2 to 4 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group with the proviso that R_1 and R_2 may not both be hydrogen or alkyl; and the pharmacologically acceptable acid-addition salts thereof; in association with a pharmaceutical carrier.

2. A composition according to claim 1 wherein the compound is a salt of sulfuric acid.

3. A composition according to claim 1 wherein the compound is a salt of hydrochloric acid.

4. A composition according to claim 1 wherein the compound is a salt of sulfamic acid.

5. A composition according to claim 1 wherein the compound is a salt of citric acid.

6. A composition according to claim 1 wherein the compound is a salt of lactic acid.

7. A composition according to claim 1 wherein the compound is a salt of succinic acid.

8. A composition according to claim 1 wherein the compound is a salt of acetic acid.

9. A composition according to claim 1 wherein the compound is a salt of gluconic acid.

10. The composition according to claim 1 wherein Q is ethylene and R_1 and R_2 are both β-hydroxyethyl and in the aromatic free base form.

11. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the disuccinate salt form.

12. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the dihydrochloride salt form.

13. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is 3-hydroxypropyl and in the dihydrobromide salt form.

14. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is 2-hydroxypropyl and in the disuccinate salt form.

15. The composition according to claim 1 wherein Q is trimethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the diacetate salt form.

16. The composition according to claim 1 wherein Q is $-CH_2CH(CH_3)-$, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the dimalate salt form.

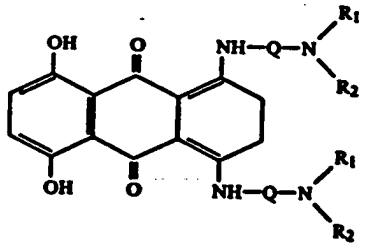
17. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the aromatic free base form.

18. A composition according to claim 17 in its pharmacologically acceptable acid-addition salt form.

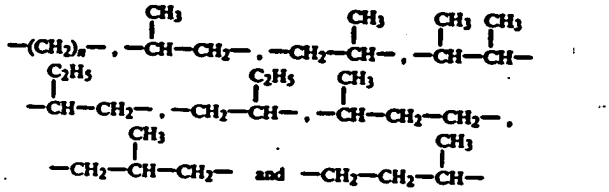
19. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the digluconate salt form.

20. The composition according to claim 1 wherein Q is ethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the dibenzoate salt form.

21. A pharmaceutical composition in dosage unit form comprising from about one to about 30 mg. of a compound selected from the group consisting of those of the formula:



wherein Q is a divalent moiety selected from the group consisting of those of the formulae:



wherein n is an integer from 2 to 4, inclusive; R_1 and R_2 are each individually selected from the group consisting of hydrogen, alkyl having from 1 to 4 carbon atoms and monohydroxyalkyl having from 2 to 4 carbon atoms and wherein the carbon atom alpha to the nitrogen atom may not bear an hydroxy group with the proviso that R_1 and R_2 may not both be hydrogen or alkyl; and the pharmacologically acceptable acid-addition salts thereof; in association with a pharmaceutical carrier.

22. A composition according to claim 21 wherein the compound is a salt of phosphoric acid.

23. A composition according to claim 21 wherein the compound is a salt of hydrobromic acid.

24. A composition according to claim 21 wherein the compound is a salt of malic acid.

25. A composition according to claim 21 wherein the compound is a salt of tartaric acid.

26. A composition according to claim 21 wherein the compound is a salt of benzoic acid.

27. A composition according to claim 21 wherein the compound is a salt of ascorbic acid.

28. The composition according to claim 21 wherein Q is ethylene, R_1 is hydrogen, and R_2 is β-hydroxyethyl and in the leuco free base form.

29. The composition according to claim 21 wherein Q is ethylene, R_1 is hydrogen, and R_2 is 2-hydroxypropyl and in the leuco free base form.

* * * * *

EXHIBIT B

UNITED STATES PATENT OFFICE

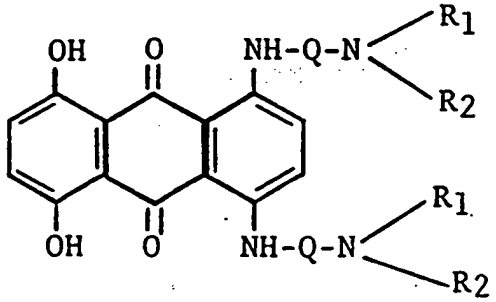
CERTIFICATE OF CORRECTION

Patent No. 4,278,689 Dated July 14, 1981

Inventor(s) KEITH CHADWICK MURDOCK and FREDERICK EMIL DURR

It is certified that error appears in the above-identified patent and that said Letters Patent are hereby corrected as shown below:

IN THE CLAIMS: Claim 1, Column 30, Lines 52-60



Signed and Sealed this

Twenty-second Day of September 1981

Attest:

Ruth M. Wroy

Attesting Officer

GERALD J. MOSSINGHOFF

Commissioner of Patents and Trademarks

EXHIBIT C

This brief description of the activities undertaken by the assignee of record of U.S. Patent No. 4278689 during the regulatory review period with respect to the approved product consists of two attachments. The first is a 109 page computer printout covering the period of IND No. 16-332 while the second is a 19 page computer printout covering the period of NDA No. 19-297. These two computer printouts list all submissions to, responses from, and transactions with the Food and Drug Administration during the regulatory review period.

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Apr-12-79			79-1	DRS		110128
			SUBMITTED INDA FOR CL 232,315. ATTACHED: PART X INCLUDES CLINICAL TRIAL PLAN FOR PHASE I AND EARLY PHASE II & PROTOCOL FOR INITIAL PHASE I STUDY TO BE CONDUCTED BY J. DURANT; PART IX INCLUDES CVs FOR DRs. DURANT, GAMS, AND MURRAY. QUALIFICATIONS & PROTOCOLS FOR EACH ADDITIONAL INVEST. WILL BE FILED BEFORE STUDY BEGINS.				
F	May-21-79				DRS		110127
			ACKNOWLEDGE RECEIPT OF INDA PERSUANT TO SECTION 505(i) AND ASSIGNMENT OF INDA NO. 16-332 FOR CL 232,315.				
L	Jun-01-79			79-2	DRS		110125
			STUDY PROPOSED FOR DR. ARNOLD CANCELLED (ADMINISTR. REASONS) & INITIAL STUDY TO BE PERFORMED BY DR. D. VON HOFF. ITEMS SUBMITTED: V REVISED QC MONOGRAPH OF CL 232,315 PARENTERAL; IX CHECKLIST & CVs FOR VON HOFF & DR. COLTMAN; X REVISED CLINICAL TRIAL PLAN & PROTOCOL FOR VON HOFF'S STUDY.				
F	Aug-06-79				DRS		110154
			REF. SUBJECT INDA, RECOMMENDATIONS & REQUESTS: MEDICAL: APPLY RADIONUCLIDE TEST FOR CARDIAC TOX. IN UNIV. OF TEXAS STUDY TO REPLACE CANCELLED STUDY AT UNIV. OF ALABAMA. CHEMISTRY: 19 REQUESTS ON SPECS. AFFECTING CONTROLS & MANUFACTURING. PHARMACOLOGY: REQUEST ANIMAL MODELS DEMONSTRATING COMPARATIVE CARDIOTOX. OF SUBJECT DRUG AND DOXORBUBICIN ETC., ANALAGOUS TO A CLINICAL SITUATION.				
F	Sep-17-79				DRS		110129

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
			re. INDA AND AMDT. OF 6/1/79. RECOMMENDATION: RADIONUCLIDE TECH. FOR CARDIAC TOX. PROPOSED IN CANCELLED PHASE I STUDY AT UNIV. OF ALABAMA SHOULD BE APPLIED TO INITIAL PHASE I STUDY AT UNIV. OF TEXAS.				
L	Sep-19-79			79-3	DRS		110130
			RESP TO FDA LETTER (8/6/79) AND SUPPLYING QUALIFICATIONS FOR NEW INVEST & PROTOCOL FOR HIS STUDY. ITEMS ATTACHED: AMEND. A, RESPONSE TO CHEM. ITEMS 1-9 (IN 8/6 LETT.); PART VI, RESPONSE TO PHARMACOLOGY REQUEST (IN 8/6 LETT.); PART IX, CHECKLIST & CVs FOR ALBERTS & HERMAN; PART X, RESPONSE FOR MURRAY TO MEDICAL RECOMMEND. (IN 8/6 LETT.); PROTO. FOR ALBERTS STUDY TO INCORPORATE CARDIAC TOX BY RADIONUCLIDE TECH.				
L	Nov-26-79			79-4	DRS		110131
			AMENDED INDA: PART IX, CHECKLIST & CVs FOR ADDITIONAL INVEST. A. LIPTON & ASSOCIATE DR. HARVEY; PART X, PROTOCOL FOR LIPTON STUDY - APPROVED BY CLINICAL INVEST. COMMITTEE. STUDY BY D. ALBERTS SUSPENDED AT REQUEST OF DR. JOHNSON (10/15). AFTER DISCUSSED SUPPORTING DATA, JOHNSON AGREED TO RESUMPTION OF STUDY. E. MCKEON OF LED. INFORMED AND STUDY NOW IN PROGRESS.				
L	Dec-04-79			79-5	DRS		110132
			re. FDA LETTER 8/6/79 CHEMISTRY (ITEM 1); REQUEST RELEASE SPECIFICATIONS ON RAW MATERIALS AS SUPPLIED BY MANUFACT. AND ANY ADDIT. CONTROLS PERFORMED BY LED. ATTACH. A, (LED. LETTER 9/19/79), INDICATED INFO. TO BE FURNISHED A.S.A.P (INCLUDED PART V). ITEMS SUBMITTED: PART V, AVAILABLE MANUFACT. RELEASE SPECS.; PART X, ADDENDA TO PROTOCOL SUBMITTED 11/2/79 FOR A. LIPTON STUDY.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND	MITOXANTRONE CL 232,315 ANTICANCER AGENT					
F	Dec-14-79				DRS		110133
			REF. INDA AND AMEND. OF 9/19 AND 11/2 AND TELE. CONVERSATION 10/15/79 BETWEEN (LED) MURRAY AND (AGENCY) JOHNSON AND 10/31/79 CONVERSATION BETWEEN (UNIV. ARIZONA) ALBERTS AND JOHNSON. AGREED 10/31, NO OBJECTION TO ALBERTS CONTINUING PHASE I STUDY PROVIDED CLOSE CONTACT WITH VON HOFF IS KEPT REGARDING DEVELOPMENTS IN HIS RELATED STUDY.				
L	Mar-04-80			80-1	DRS		110134
			AMENDED INDA: PART IX, CHECKLIST AND CVs FOR J. HOLCENBERG AND T. VIETTI, AND DRs. FUSNER, LAND & BHANOT; PART X, PROTOCOL FOR HOLLENBERG STUDY, PROTOCOL FOR VIETTI STUDY, & ADDENDA TO PROTOCOL SUBMIT. 9/19/79 FOR ALBERTS STUDY.				
L	Apr-30-80			80-2	DRS		110135
			AMENDED INDA: PART IX, CHECKLIST OF CURRENTLY ACTIVE INVESTIGATORS; PART X, ANNUAL PROGRESS REPORT.				
L	Jun-20-80			80-3	DRS		110136
			AMENDED INDA: PART IX, CVs DRs. WYNERT AND SIMMONDS, ASSOCIATES WITH LIPTON AND STUDY FILED 10/4/79; PART X, CLINICAL REPORT FOR VON HOFF STUDY.				
L	Aug-19-80			80-4	DRS		110137
			AMENDED. INDA PROVIDE FOR PHASE II STUDIES. CLINICAL TRIAL PLAN DESCRIBES ARRANGE. WITH NCI FOR ONCOLOGY GROUP STUDIES. ITEMS INCLUDED: PART VI, ADDITIONAL PRECLINICAL STUDIES; PART VII, UPDATED INVEST BROCHURE; PART IX, UPDATED CV FOR VON HOFF (ORIGINALLY LISTED AS AN INVEST 6/1/79); PART X, CLINICAL TRAIL PLAN, 7 PROTOCOLS FOR PHASE II STUDIES, CLINICAL REPORT FOR ALBERTS STUDY.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Oct-08-80			80-5	DRS		110138
			AMENDED INDA: PART I, USAN NOMENCLATURE STATEMENT; PART X, ADDENDUM TO PROTOCOL SUBMIT. 11/2/79 FOR LIPTON STUDY (EARLIER ADDENDA FILED 12/4/79). ALSO, TAYLOR PHARMACAL CO., ILL. CONTRACTED TO MANUFACT. & PACKAGE CL 232,315 FOR LED. EXHIBIT I, MANUFACT. & CONTROL DOCUMENT. & GMP STATEMENT. BOTTLES & FINISHED STOCK TO LED. FOR QC RELEASE TEST PRIOR TO CLINICAL TRIAL.				
L	Oct-22-80			80-6	DRS		110139
			AMENDED INDA: PART IX, CVs DRs. BERGAMINI AND SEDLIS TO ASSIST T. VIETTI; PART X, AMEND. TO PROTOCOL SUBMIT. 3/4/80 FOR HOLCENBERG STUDY.				
L	Nov-13-80			80-7	DRS		110140
			AMENDED INDA: PART IX, UPDATED CV FOR D. ALBERTS & CVs FOR DRs. WOOLFENDA, PATTON AND AAPRO TO ASSIST ALBERTS; PART X, PROTOCOL FOR ALBERTS NEW STUDY. PROTOCOL AMEND. FILED 10/22/80 FOR HOLCENBERG STUDY ALSO APPLIES TO VIETTI STUDY SUBMIT. 3/4/80.				
L	Nov-24-80			80-8	DRS		110141
			AMENDED INDA: PART IX, CHECKLISTS AND CVs FOR 27 ADDITIONAL INVEST., UPDATED CV FOR VON HOFF. ALL INVESTIGATORS WILL FOLLOW 7 PHASE II PROTOCOLS SUBMIT. 8/19/80 AND WILL REPORT THROUGH VON HOFF.				
L	Dec-16-80			80-9	DRS		110142
			AMENDED INDA: PART X, TWO ADDITIONAL PROTOCOLS FOR PHASE II STUDIES AND REPORTED THROUGH VON HOFF. MEMBERS OF GROUP NAMED IN SUBMISSION OF 8/19/80 AND 11/24/80.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Feb-06-81			81-1	DRS		110143
			AMENDED INDA: PART III, FORMULAS; PART VII, LABELS; PART X, ADDITIONAL PROTOCOL FOR PHASE II STUDIES, AND REPORTED THROUGH VON HOFF. MEMBERS OF GROUP NAMED IN SUBMISSION OF 8/19/80 AND 11/24/80, AMEND. TO PROTOCOL FOR HOLCENBERH & VIETTI SUBMIT. 3/4/80 AND AMENDED 10/22/80.				
L	Mar-31-81			81-2	DRS		110144
			AMEND INDA: PART III, FORMULA; PART IV, SYNTHESIS RADIOLABELED MITOX.; PART VII, LABELING; PART IX, CHECKLIST SHOWING 3rd STUDY BY ALBERTS (QUALIFICATION SUBMIT 11/13/80), CHECKLISTS 21 ADDIT. INVEST & THEIR CVs, CV FOR DAVIS (ASSOCIATE ALBERTS); PART X, PROTOCOL ALBERTS NEW STUDY, 10 PROTOCOLS FOR PHASE II STUDIES, RESULTS REPORTED THROUGH GAMS, 3 PROTO. FOR PHASE II AND REPORT THROUGH VON HOFF, CLINICAL REPORT FOR LIPTON STUDY.				
L	Apr-10-81			81-3	DRS		110145
			AMENDED INDA: PART V, ADDIT. STABILITY DATA; PART IX, CHECKLIST FOR ADDITIONAL INVEST. J. ALLEGRA, AND REPORTED THROUGH GAMS, REVISED CHECKLIST NAMING D. WOODWARD MONITOR FOR ALBERTS STUDY SUBMITTED 3/31/81, CV FOR ALLEGRA AND WOODWARD.				
L	Jun-02-81			81-4	DRS		110146
			AMENDED INDA: PART IX, CHECKLIST OF CURRENT ACTIVE INVEST., CV FOR T. TERZAKIS; PART X, ANNUAL PROGRESS REPORT, AMEND. TO VON HOFF PHASE I STUDY (SUBMIT. 6/1/79), VON HOFF STUDY REPORT.				
L	Jun-08-81			81-5	DRS		110147

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			AMENDED INDA: PART IX, CHECKLIST AND CV FOR ADDITIONAL INVEST. J. NEIHART AND CVs FOR ASSOCIATES DRs. MISER AND MALSPEIS; PART X, PROTOCOL FOR NEIDHART STUDY, AMEND. TO HOLCENBERG AND VIETTI STUDIES SUBMIT. 3/4/80 AND AMENDED 10/22/80 AND 2/6/81.				
L	Jul-08-81			81-6	DRS		110148
			AMEND INDA: PART VII, UPDATE BROCHURE FOR INVEST, SAMPLE LETTER WITH ATTACH FROM LEV DESCRIBING INCIDENTS OF CARDIOTOX IN PATS TREATED WITH MITOX. LETTER SENT TO ALL LED INVEST & NCI NOTIFED BY LEV; PART IX, UPDATED CV VIETTI; PART X, AMEND TO PROTOCOL FOR HOLCENBERG & VIETTI STUDIES SUBMIT 3/4/80 & AMEND 10/22/80, 2/6 & 6/8/81, PROT FOR PHASE II STUDY BY POG, HOLCENBERG & VIETTI COMBINE CLIN REP, ADDENDUM LIPTON REP SUBMIT 3/31/81.				
L	Jul-31-81			81-7	DRS		110151
			AMENDED INDA: PART VI, ADDIT. PRECLINICAL STUDIES; PART VII, SAMPLE LETTER WITH ATTACH. FROM LEV SUMMARIZING 9 CASES OF CARDIOTOX. ASSOCIATED WITH MITOX. & LISTING NEW ENROLL. RESTRICTIONS - SENT TO ALL LED. INVEST.; PART IX, CVs FOR DRs. BERGAMINI, DISTELHORST, LAND, & SEDLIS (ASSOC. TERESA); PART X, REPORT OF AN ADVERSE EXPERIENCE (ONE DESCRIBED IN LEV'S LETTER 7/14/81).				
L	Sep-08-81			81-8	DRS		110149
			AMENDED INDA: PART X, PROTOCOL AMEND. TO ONGOING MITOXANTRONE STUDIES INITIATED BY NCI DUE TO REPORTS OF CARDIOTOX., REPORT OF AN ADVERSE EXPERIENCE.				
L	Oct-23-81			81-9	DRS		110157
			AMENDED INDA: PART X, AMEND. TO PROTOCOL SUBMIT. 3/31/81 FOR ALBERTS STUDY.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE CL 232,315 ANTICANCER AGENT					
F	Oct-26-81				DRS		110152
			REF. INDA: REPORTED 20 CASES CONGESTIVE HEART FAILURES IN PAT. RECEIVING MITOX. REQUIRING A COMPREHENSIVE PLAN FOR FUTURE STUDIES. THIS SUBMISSION SHOULD ACT AS INTERIM PROGRESS REPORT TO INCLUDE TOTAL NO. PAT. ENTERED TO DATE, TUMOR RESPONSE & TYPE OF DOSE SCHED., LIST ALL STUDIES & WHICH STILL OPEN, & INFO. ON TOX. i.e. MOST FREQUENTLY SEEN AND PERCENT OF PAT. OCCUR. REQUEST ALSO BEING MADE OF NCI.				
L	Nov-30-81			81-10	DRS		110153
			RESPONSE TO FDA CORRES. 10/26/81 REGARDING EFFICACY AND SAFETY OF MITOX. ATTACHED REPORT ID'S SOURCES OF DATA AND NO. PATS. INVOLVED. MORE DETAILED REPORT TO BE SUPPLIED BY JANUARY. DRs. ALBERTS AND NEIDHART STUDIES ARE CURRENTLY ACTIVE.				
L	Dec-30-81			81-11	DRS		110150
			AMENDED INDA: PART V, QC MONOGRAPH & RELATED ANALYT. RESEARCH METHOD REPORT 78, UPDATE HPLC ASSAY BULK DRUG SUBSTANCE & PARENT. PREPS.; PART IX, CV & CHECKLIST FOR D. McDONALD, CV FOR R. FOWLER (ASSIST. McDONALD); PART X, PROTOCOL FOR 2 STUDIES BY McDONALD, PROTOCOL FOR PHASE II-III STUDY CONDUCTED BY SWOG & REPORTED THROUGH VON HOFF, AMEND TO PREVIOUS SUBMIT. SWOG PROTOCOLS.				
L	Mar-04-82			82-1	DRS		110155
			AMENDED INDA: PART IX, CHECKLIST AND CV FOR ADDITIONAL INVEST. J. STURGEON; PART X, PROTOCOL AND CRF FOR STURGEON STUDY, REPORT OF ADVERSE EXPERIENCE IN NCI-SPONSORED STUDY.				
L	Mar-17-82			82-2	DRS		110156

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			AMENDED INDA: PART IX, CV M. FUJIMORI TO MONITOR STUDIES PREVIOUSLY ASSIGNED TO MURRAY OR TERZAKIS. WOODWARD & FOWLER CONTINUE TO MONITOR STUDIES INDICATED ON CHECKLIST AT TIME OF PROTOCOL FILING.				
L	Mar-26-82			82-3	DRS		110158
			REF. FDA CORRES. 10/26/81 AND LED. RESPONSE 11/30/81. REPORT SUMMARIZ. SAFETY & EFFICACY DATA FOR MITOX. SUBMITTED. ITEMS ATTACHED: PART X, MITOX. REPORT, PROPOSED CLIN. OPERATING PLAN, DRUG EXPERIENCE REP. FROM ALBERTS CARDIAC FUNCT. STUDY (LED. SPONSOR), DRUG EXPERIENCE REP. FROM PAT. IN NCI-SPONSORED STUDIES. REQUEST FOR MEETING TO DISCUSS FUTURE CLIN. STUDIES WITH MITOX.				
L	Apr-20-82			82-4	DRS		110159
			AMENDED INDA: PART VI, ADDITIONAL PRECLINICAL STUDIES; PART X, FD FORM 1639 FILED 3/4/82 FOR PAT. B.B., #54585. DISCUSSION OF CARDIAC DIFFICULTIES AND "NOT CONTRIBUTING TO DEATH". AFTER FURTHER REVIEW, RELATIONSHIP WOULD BE CLASSIFIED AS "POSSIBLE". (SEE LETTER FOR MORE DETAILED DESCRIPTION OF CARDIAC DIFFICULTIES.)				
L	May-06-82			82-5	DRS		110126
			AMENDED IND SUBMIT.: IX, CHECKLIST OF CURRENTLY ACTIVE INVEST.; X, ANNUAL PROGRESS REPORT.				
L	May-25-82			82-6	DRS		111759
			IN ANTICIPATION OF 6/23/82 MEETING, SUBMIT 1)PROSPECTIVE CLINICAL OPERATING PLAN, 2)PROTOCOL FOR STUDY IN PATIENTS WITH BREAST CANCER.				
L	Jun-07-82			82-7	DRS		110351

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			AMEND. SUBJECT INDA: PART VII, REVISED BROCHURE FOR INVEST.; PART IX, CHECKLIST STUDY BY YAP (BODEY CO-INVEST.), CVs YAP & BODEY AND ASSOC. BLUMENSCHEIN, EWER, BENJAMIN, HORTOBAGYI, SCHELL, AND WALLACE; PART X, PROTOCOL FOR YAP AND BODEY STUDY.				
L	Jun-11-82			82-8	DRS		110515
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CV FOR ROWAN & ASSISTANTS TONG & BLOCK; PART X, PROTOCOL FOR CHLEBOWSKI'S STUDY.				
L	Jun-14-82			82-9	DRS		110514
			PURSUANT TO TELE. CONVERSATION WITH JOHNSON(FDA) 6/9/82, SENDING ADDITIONAL PROTOCOLS FOR REVIEW PRIOR TO MEETING 6/23. CALL ATTENETION TO PROTOCOL SUBMIT 6/7/82 FOR YAP & BODEY STUDY (ITEM 5 ON TABLE 1 OF PROSPECTIVE CLIN. OPERATING PLAN).				
L	Jul-13-82			82-10	DRS		110832
			AMEND SUBJECT INDA: PART VII, PHARMACY BROCHURE; PART IX, CHECKLIST & CVs FOR SILVER LEVICK GRACE ALLEGRA WOODCOCK & WOLFF, CV FOR ASSISTS PASMANTIER COLEMAN NACHMAN JAROWSKI SOLF RUGGIERO RESNICK CHIARIERI SALETAN MOLANDER(SILVER), LEVICK DESAI(LEVICK), JOHNSTON SARG(GRACE), KUBOTA RICHMAN BLUMENREICH(ALLEGRA), & GRECO HAINSWORTH BRENNER HANDE(WOLFF); PART X, PROT & CRF FOR MULTI-CENTER STUDY, DRUG EXPERI FROM NCI STUDY.				
L	Jul-15-82			82-11	DRS		110827
			SUBMIT TO SUBJECT INDA PACKAGE 2 DRUG EXPERIENCE REPORTS FROM NCI STUDIES OMITTED FROM 7/13/82 SUBMIT.				
L	Jul-22-82			82-12	DRS		111760

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CV FOR 5 NEW INVESTIGATORS & CVs FOR THEIR ASSOCIATES (REF HARD COPY LETTER FOR LIST OF NAMES); PART X, DRUG EXPERIENCE REPORT. FIVE NEW INVEST TO FOLLOW PROTOCOL SUBMIT 7/13/82.				
L	Jul-29-82			82-13	DRS		111062
			AMEND SUBJECT INDA: CHECKLIST & CVs FOR SPICER, PERLOFF & DUGAN, CVs FOR MITCHELL, ARDALAN, BERTRAM, GRUNBERG, KEMPF, & DANIELS (ASSIST SPICER), CVs FOR ELLISON, HYMAN, OSTER, STOOPLER, & RAPOPORT (ASSIST PERLOFF), CVs FOR SCHROEDER, BATES, & WORKMAN(ASSIST DUGAN); PART X, EXPLAIN CARDIOTOX MONITOR FOR STURGEON STUDY(SUBMIT 3/4/82). 3 INVEST ABOVE TO FOLLOW PROT SUBMIT 7/13/82.				
L	Aug-05-82			82-14	DRS		111092
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CV FOR ROSS, CV FOR KRAMER (ASSIST ROSS). ROSS TO FOLLOW PROTOCOL SUBMIT 7/13/82.				
L	Aug-19-82			82-15	DRS		111185
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CVs FOR MOORE, DAO & VOLBERDING, CVs FOR NEMOTO & PATEL (ASSIST DAO), CV FOR GENTILE (ASSIST ALLEGRA & WOODCOCK IN STUDY SUBMIT 7/13/82); PART X, AMEND TO PROTOCOL TO AFFECT DAO'S STUDY ONLY. ALL INVEST TO FOLLOW PROTOCOL SUBMIT 7/13/82.				
L	Aug-24-82			82-16	DRS		111222
			AMEND SUBJECT INDA: PART IX, CHECKLIST & UPDATED CV FOR NEIDHART & CVs FOR ASSOC BALCERZAK, BOURONCLE, DEWALD, GREVER, KRAUT, METZ, RINEHART, ROACH, SOGONE, WALL, & WILSON; PART X, PROT FOR NEIDHART STUDY & SAMPLE COMPUTER CRF. SPONSOR FOR 1st NEIDHART STUDY (ON SINCE 11/80) TRANSFER FROM NCI TO LED. DETERMIN OF PHARMACOKINETIC PARAMETER DELETED FROM PROT OBJECTIVE. UPDATED TOX STUDIES INCLUDED.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Sep-03-82			82-17	DRS		111245
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CVs FOR DOTY & GOLOMB, CVs FOR KANE & REGAN (ASSIST DOTY), CVs FOR ALBAIN, BARON, GAYNOR, HOFFMAN, LARSON, NEELY, PEARSON, ULTMANN, VAN SHEPARD, & WADE (ASSIST GOLOMB). DOTY & GOLOMB TO FOLLOW PROTOCOL SUBMIT 7/13/82.				
L	Sep-10-82			82-18	DRS		111250
			AMEND SUBJECT INDA: PART IX, CHECKLIST FOR SILVER 2nd STUDY (QUALIF SUBMIT 7/13/82), CHECKLIST & CVs FOR ARMENTROUT, BROUN, & GOLDMAN, CVs FOR BROWER & MOORE (ASSIST SILVER), STATER (ASSIST ARMENTROUT), GALLAGHER, JOIST, D.LUEDKE, S.LUEDKE, & PETRUSKA (ASSIST BROUN), GRADY, BURNINGHAM, GALEN (ASSIST GOLDMAN); PART X, PROT TO BE FOLLOWED BY SILVER, ARMENTROUT & BROUN. GOLDMAN TO FOLLOW PROT SUBMIT 7/13/82.				
L	Sep-17-82			82-19	DRS		111277
			AMEND SUBJECT INDA: PART IX, CHECKLIST FOR COSTANZI 2nd STUDY, CHECKLIST & CV FOR ERSLEV, UPDATED CV FOR COSTANZI, CHECKLIST FOR BLOCK (QUALIF FILED 6/11/82), CVs FOR ALPERIN GARDNER, GUPTA, & WEISS (ASSIST COSTANZI), CVs FOR 10 ERSLEV'S ASSOCIATES (SEE HARD COPY FOR NAMES). BLOCK TO FOLLOW PROT SUBMIT 7/13/82. COSTANZI & ERSLEV FOLLOW PROT SUBMIT 9/10/82.				
L	Sep-29-82			82-20	DRS		111320
			REF SUBJECT INDA; SUBMIT NOTED FROM 6/23/82 MEETING WITH FDA.				
L	Oct-01-82			82-21	DRS		111323

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CV FOR ARLIN & CVs FOR ASSIST CLARKSON, GEE, KEMPKIN, MERTELSMANN, & STRAUS. ARLIN TO FOLLOW PROTOCOL SUBMIT 9/10/82.				
L	Oct-07-82			82-22	DRS		111347
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CVs FOR WHITE, BITRAN, & AMARE, CVs FOR BILLINGS, DESSER, KOSLOFF, NEWMAN, ROBIN, SHAPIRO, & SWEET (ASSIST BITRAN), CVs FOR BODENSTEINER, COOK, LYNCH, & SKIKNE (ASSIST AMARE); PART X, AMEND TO PROT FOLLOWED BY SILVER, ALLEGRA, WOODCOCK, & PERLOFF. WHITE & BRITTAN TO FOLLOW PROT SUBMIT 7/13/82, AMAR FOLLOW PROT SUBMIT 9/10/82.				
L	Oct-18-82			82-23	DRS		111358
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CVs FOR STARLING, MISER, MULNE, & MILLER, CV FOR FERNBACH, MAHONEY & STEUBER (ASSIST STARLING), CV FOR NEWTON, ROACH & RUYMANN (ASSIST MISER & MULNE), CV FOR HOFFMAN & TAN (ASSIST MILLER); PROTOCOL & CRF FOR MULTICENTER STUDY.				
L	Oct-25-82			82-24	DRS		111368
			AMEND SUBJECT INDA: PART IX, CHECKLIST FOR ADDITIONAL STUDY BY GAMS, CHECKLIST & CV FOR CASSELETH AND VATS, CV FOR THUEWORTHY (ASSIST VATS), UPDATED CV FOR GAMS. GAMS & CASSILETH TO FOLLOW PROTOCOL SUBMIT 9/10/82. VATS TO FOLLOW PROTOCOL SUBMIT 10/18/82.				
L	Nov-08-82			82-25	DRS		111402
			AMEND SUBJECT INDA: PART IX, CHECKLIST FOR 2nd MOORE STUDY (QUALIF SUBMIT 8/18/82); PART X, AMEND TO REIDHART PROTOCOL SUBMIT 8/24/82, DER FOR BOTH LED AND NCI SPONSORED STUDIES. MOORE TO FOLLOW PROTOCOL SUBMIT 9/10/82.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Dec-03-82			82-26		DRS	111461
			AMEND SUBJECT INDA: PART IX, CV FOR BERNHARDT (ASSIST SILVER); PART X, ADDENDUM TO PROTOCOL SUBMITTED 7/13/82.				
L	Dec-08-82			82-27		DRS	111465
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CVS FOR PETERSON & STEIN, CVS FOR BARNES, BLOOMFIELD, HRUSHESKY, HURD, KENNEDY, KENYON, AND KIANG (PETERSON ASSOC); PART X, PROTOCOL TO BE FOLLOWED BY PETERSON & STEIN.				
L	Dec-13-82			82-28		DRS	111445
			AMEND SUBJECT INDA: PART IX, CV FOR DUKART TO REPLACE FUIJIMORI AS LED MONITOR; PART X, AMEND TO PROTOCOL SUBMITTED 6/7/82.				
F	Dec-29-82		TELEPHONE CALL DR.JOHNSON TO DR.B.J.CLARK (CONFM 1/10/83)			DRS	830034
			(a) PROTOCOL Questioned 1st line therapy for non-Hodgkins lymph				
L	Jan-04-83		AMENDMENT	83-1		DRS	830163
			(a) CV,CKLST PT9 /003-046-006 DP3-46 SUBM 12/8/82, AMENDED 6/21/83 GAMS,RICHARD A LYMPHOMA NON-HODGKIN'S				
			AMEND SUBJECT INDA: PART IX, CHECKLIST & UPDATED CV FOR GAMS. GAMS TO FOLLOW PROTOCOL SUBMITTED 12/8/82.				
L	Jan-10-83	F Dec-29-82	AMENDMENT RIVKIN STUDIES	83-2		DRS	830021

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(b) PROTOCOL
PT10 /003-046-010
No patients on 1st line therapy
(c) PROTOCOL # /PT 10
DP 3-44 dosage amended,originally submitted 9/10/82

AMEND SUBJECT INDA: PART IX, CHECKLIST FOR SILVER THIRD STUDY, CV FOR 2 ADDITIONAL ASSOCIATES MOORE AND WOLF; PART X, AMEND TO PROT SUBMIT 9/10/82. SILVER TO FOLLOW PROT SUBMIT 10/8/82.

F Feb-04-83 DRS 830135
6/7/82 MESTASTIC BREAST CA;12/8/82 NON-HODGKINS LYMPH SUBMIS

(a) PROTOCOL
Exclude Novantrone as single agent w/non-Hodg lymp
(b) INVEST BROCH
2/82,pg116:clar eliq,monit prior heart dis,cardiomyopathy

REF APPLICATION FOR INDA & LED CORRES 6/7 & 12/8/82. APPROVE INITIATION OF CLIN TRIALS. HAVE FOLLOWING RECOMMENDATIONS: (1)IN PROT SUBMIT 12/8/82, SHOULD MODIFY TO EXCLUDE AS FIRST LINE THERAPY, PAT WITH NON-HODGKINS LYMPHOMA, AND (2)CLINICAL BROCHURE SHOULD STATE ELIGIBILITY RESTRICTIONS REGARDING PRIOR HEART DISEASE.

L Feb-09-83 AMENDMENT 83-6 DRS 830130
SARTIANO/BODEY STUDIES

(a) CV(& ASSOCs),CKLST,PROT
PT9,10 /003-047-001
BODEY,GERALD P
(c) CKLST,CV-ASSOC(s) /003-040-0
PROT SUBM 7/13/82
SARTIANO,GEORGE P
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS

AMEND SUBJECT INDA: PART IX, CHECKLIST FOR 2ND SARTIANO STUDY, CHECKLIST FOR NEW BODEY STUDY. UPDATED CV FOR BABCOCK (ASSOCIATE OF SRATIANO), CVs FOR BURGESS, ESTEY, LEGHA, & VALDIVIESO (ASSIST BODEY); PART X, PROTOCOL FOR BODEY STUDY. SARTIANO TO FOLLOW PROTOCOL SUBMIT 7/13/82 AND AMENDED 1/10/83.

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Feb-14-83		AMENDMENT	83-7	DRS		830124

KREMENTZ/VOGEL/HOLLAND/PLOTKIN/MUGGIA STUDIES

(a) CKLST & PROTOCOL
PT9,10 /003-048-004
KREMENTZ,EDWARD T
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(b) CV,CKLST,PROTOCOL
PT9,10 /003-055-001
HOLLAND,JAMES F
ALL
COMBINED w/ VINCRISTINE & DEXAMETHASONE

(c) CV,CKLST,PROTOCOL
PT9,10 /003-048-001
MUGGIA,FRANCO
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(d) CV,CKLST,PROTOCOL
PT9,10 /003-048-005
PLOTKIN,DAVID
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(e) CV,CKLST,PROTOCOL
PT9,10 /003-048-002
VOGEL,CHARLES L
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(f) CV # /PT 9
Assoc:Dr.Wang

(g) CV # /PT 9
Assoc:Drs.Cuttner,Harris,Ohnuma,Paciucci

(h) CV # /PT 9
Assoc:Drs.Carter,Sutherland

(i) CV # /PT 9
Assoc:Drs.Blum,Bottino,Green,Levin,Speyer,Spiegel,
Wernz

AMEND SUBJECT INDA: PART IX, CHECKLIST FOR DREMENTZ SECOND STUDY, CHECKLIST & CVs FOR BOGEL, HOLLAND, PLOTKIN, AND MUGGIA, UPDATED CV FOR CARTER & SUTHERLAND, CVs FOR VOGEL, HOLLAND & MUGGIA ASSOCIATES (SEE HARD COPY FOR NAMES); PART X, PROT FOR VOGEL, KREMENTZ, PLOTKIN, & MUGGIA STUDIES, PROT FOR HOLLAND STUDY.

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Feb-24-83			83-8		DRS	111629
			AMEND SUBJECT INDA: PART IX, CHECKLIST AND CVs FOR BYRNE & JUSS, CV FOR WOOLLEY (ASSIST BYRNE), CVs FOR PASCHOLD, CAPONERA & POPE (ASSIST MUSS), CV FOR BRAICH (ASSIST JONES IN STUDY SUBMIT 1/25/83). BYRNE & MUSS TO FOLLOW PROTOCOL SUBMIT 2/14/83.				
L	Mar-02-83			83-9		DRS	111663
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CV FOR DESAI, CV FOR DIMITROV TO ASSIST NEIDHART. DESAI WILL FOLLOW PROTOCOL SUBMIT 2/14/83. MULNE WILL BE ASSUMING RESPONSIBILITY FOR PROTOCOL STUDY SUBMIT 10/18/82 FOR MISER.				
L	Mar-04-83			83-10		DRS	111664
			AMEND SUBJECT INDA: PART IX, CVs FOR BODEY'S ASSISTANTS ON STUDY PROTOCOL SUBMIT 2/9/83 (REF HARD COPY LETTER FOR NAMES).				
L	Mar-07-83			83-11		DRS	111666
			AMEND SUBJECT INDA: PART IS, CHECKLIST & CVs FOR DECONTI & BRODOVSKY, CVs FOR BYRNE, DAVIS, FLATOW, HETZEL, ROSS, STEINGART, & WHITE (ASSIST DECONTI), CVs FOR LAUCIUS & HOLROYDE (ASSIST BRODOVSKY). DECONTI & BRODOVSKY TO FOLLOW PROTOCOL SUBMIT 2/14/83.				
L	Mar-17-83			83-12		DRS	111690
			AMEND SUBJECT INDA: PART IX, CHECKLIST FOR 3rd GOLOMB STUDY, CHECKLIST & CV FOR PAPISH & ASSOCIATES KRITZMAN, MIER, MILLER, PARKINSON, RUDDERS, & TAYLOR, CV FOR LESTER & VOGELZANG (ASSIST GOLMB). GOLOMB & PAPISH TO FOLLOW PROTOCOL SUBMIT 2/14/83. ACKNOWL RECEIPT FDA 2/4/83 LETTER AND IMPLEMENTING RECOMMENDATIONS MADE.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Mar-22-83			83-13	DRS		111701
			AMEND SUBJECT INDA: PART IX, CHECKLIST SHOWING NEW STUDY FOR GAMS & CV FOR ASSOCIATES PERLMAN AND KARDINAL. GAMS TO FOLLOW PROTOCOL SUBMIT 2/14/83.				
L	Mar-31-83			83-14	DRS		111715
			AMEND SUBJECT INDA: PART IX, CHECKLIST & CVs FOR BENNETT & DOROSHOW, CV FOR BAKEMEIER, CARIGNAN, & MCCUNE (ASSIST BENNETT), CV FOR BERTRAND, BROWNING, CARR, & OVERBY (ASSIST DOROSHOW), CHECKLIST SHOWING ADDRESS CHANGE FOR ARLIN, UPDATED CV FOR ARLIN. BENNETT & DOROSHOW TO FOLLOW PROTOCOL SUBMIT 2/14/83.				
L	Apr-06-83			83-15	DRS		111750
			AMEND SUBJECT ANDA: PART IX, CHECKLIST FOR HOLLAND 2ND STUDY; PART X, PROTOCOL FOR HOLLAND NEW STUDY.				
L	Apr-22-83		AMENDMENT PROTOCOL SUPPLEMENT TO GAM'S STUDY IN ADULT LEUKEMIA	83-16	DRS		830226
			AMEND SUBJECT INDA: PART X, PROTOCOL SUPPLEMENT TO GAM STUDY SUBMIT 9/10/82.				
L	May-11-83		AMENDMENT SCHEIN ASSISTING BYRNE IN STUDY FILED 2/24/83	83-17	DRS		830285
			AMEND SUBJECT INDA: PART IX, CV FOR SCHEIN TO ASSIST BYRNE IN STUDY FILED 2/24/83.				
L	May-27-83		AMENDMENT BERTINO/BENNETT STUDIES	83-18	DRS		830343
L	Jun-13-83		AMENDMENT	83-19	DRS		830382

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(a) PROG RPT & CKLST # /PT 9,10				
L	Jun-15-83		AMENDMENT MULTICTR NON-HODGKIN'S LYMPH STUDY	83-20	DRS		830433
			(a) CKLST # /PT 9 ERSLEV,ALLAN J				
L	Jun-21-83		AMENDMENT AMEND TO MULTICTR NON-HODGKIN'S LYMPHOMA PROTO SUB 12/8/82	83-21	DRS		830483
L	Jun-24-83		AMENDMENT	83-22	DRS		830496
L	Jun-29-83		AMENDMENT HENDERSON STUDY	83-23	DRS		830502
L	Jul-06-83		AMENDMENT	83-24	DRS		830560
			(a) DRUG EXPER RPT # /PT 10 NCI-Sponsored Study				
L	Jul-25-83		AMENDMENT	83-25	DRS		830628
			(a) CV,CKLST # /PT 9 MULTI-CENTER BREAST CANCER PROTOCOL SUBMT'D 2/14/83 MORGAN,LEE ROY CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
L	Jul-29-83		AMENDMENT CV'S VARIOUS ASSTS; HOLLAND STUDY	83-26	DRS		830635
			(a) PROTOCOL PT9,10 /003-065-001 HOLLAND,JAMES F LYMPHOMA COMBINED W/ VINCRISTINE & DEXAMETHASONE				
L	Aug-08-83		AMENDMENT	83-27	DRS		830645

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(a) CV & PROTOCOL # /PT 9 PROTOCOL SUBM 7/29/83 HOLLAND,JAMES F (b) CV & PROTOCOL # /PT 9 7/29/83 SUBM CORRECTION: CV SUBM 3/31/83; STUDYING AC LEUKEM				
L	Aug-09-83		AMENDMENT	83-28	DRS		830646
			(a) CV # /PT 9 DR GAMS' ASSISTANTS IN BREAST CA STUDY (b) INVEST SITE ADDITIONAL SITE FOR AC MYELOBLASTIC LEUKEMIA STUDY WIERNIK,PETER H LEUKEMIA				
L	Aug-12-83		AMENDMENT	83-29	DRS		830654
			MULTICENTER BREAST CA STUDY (a) CV # /PT 9 ASS'T TO DR J. EVERETT				
L	Aug-17-83		AMENDMENT	83-30	DRS		830663
			(a) CKLST /003-048-0 REPLACES DECONTI; PROT 3-48 SUBM 2/14/83; CV SUBM 3/7/83 WHITE,CHARLES F CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU (b) PROTOCOL EMERGENCY TREATMENT BESIDES FORMAL STUDY (d) CV-ASSOC(s) /003-048-0 test ??? MUST WE HAVE INDIVIDUAL RR6-RR7 RECORDS FOR EACH??				
L	Aug-26-83		AMENDMENT	83-31	DRS		830698
			(a) PROTOCOL # /PT 10 AMEND TO AC MYELOBL LEUK PROT SUBMD 4/6/83 (b) PROTOCOL AMEND TO REFRACTORY LYMPHOMA STUDY SUBMITTED 7/29/83				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Aug-30-83		AMENDMENT	83-32	DRS		830692
			(a) CV(& ASSOCs),CKLST PT9 /003-040-025 PROT SUBM 7/13/82, AMENDED 1/10/83 BERNARD,STEPHEN A CA-BREAST; vs ADRIAMYCIN MULTI-CTR 2nd LINE PTS				
L	Sep-07-83		AMENDMENT	83-33	DRS		830705
			(a) FORMULA # /PT 3 (b) MONOGRAPH # /PT 5 CONTROLS (c) STABILITY # /PT 5 (d) LABEL # /PT 7 (d) LABEL # /PT 7 (e) CV # /PT 9 ASSISTANTS TO DRS R GAMS, E KREMENTZ				
L	Sep-12-83		AMENDMENT		DRS		830732
			(a) CV CV'S FOR DR DENNETT'S ACCOCIATES				
L	Sep-14-83		CORRESPONDENCE REQUEST 1-A IND/NDA CLASSIFICATION		DRS		830736
			(a) SUMMARY NOTES FROM 5/3/83 LED-FDA MTG: MTX'S ADVNTGS OVER EXIST THER (b) SUMMARY DR CLARK PROFILE OF MTX: SAF/EFFIC IN TREATING ADV BREAST CA				
L	Oct-06-83		AMENDMENT	83-36	DRS		830785
			(a) CV # /PT 9 CV FOR DR BODEY'S NEW ASST -FORMER COINVSGTR,DR YAP, LEAVES				
L	Oct-10-83		AMENDMENT	83-37	DRS		830787
			(a) CV,CKLST CV'S FOR DR ARLIN & ASSOC'S. ADD'L ASSOC CV SUBM 3/31/83				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			ARLIN,ZALMEN A CA-BREAST; vs ADRIAMYCIN MULTI-CTR 2nd LINE PTS				
L	Oct-20-83		AMENDMENT PART 10-AMNDMT TO PHASE I-II PROT (DP 3-55) SUBM 2/14/83	83-38	DRS		830815
L	Oct-25-83		AMENDMENT ADD'L PRE-CLINICAL STUDIES, PART 6	83-39	DRS		830828
L	Oct-28-83		AMENDMENT	83-40	DRS		830840
			(a) CV,CKLST # /PT 9 CKLST FOR DR ELLISON (CV SUBM 10/6/83) & CV'S FOR HER ASSOCS				
			(b) CV # /PT 9 DR TESTER (DR LEVICK'S ASSOC); DR GREENBERG (BLOCK'S ASSOC)				
			(c) SUMMARY # /PT 9 DR ELLISON REPLACES DR PERLOFF (LEFT) AS PRINC INVSGTR				
L	Oct-31-83		CORRESPONDENCE REQUEST COMMENTS ON PROSPECTIVE PROTOCOLS(2) & CLIN STRATEGY	83-41	DRS		830843
L	Nov-02-83		AMENDMENT	83-42	DRS		830853
			(a) CV,CKLST,PROTOCOL PT9 /003-000-000 WEINER,MARTIN J				
L	Nov-09-83		AMENDMENT	83-43	DRS		830867
			(a) PROTOCOL # /PT 10 REVISIONS (SECTNS 4.25 & 6.52) TO DR RODEY'S PROT SUB 6/7/82				
L	Nov-11-83		AMENDMENT	83-44	DRS		830875
			(a) CKLST,CV-ASSOC(s) PT9a /003-048-009 DP3-48 SUBM 2/14/83, AMND' 2/28/84; CV SUB4 3/17/83				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			PARKINSON,DAVID R CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			(c) PROTOCOL /003-044-0 BERTINO'S CV AND CKLST SUBM 5/27/83; ONE PT-COMPASSION BASIS BERTINO,JOSEPH LEUKEMIA				
L	Nov-30-83		AMENDMENT	83-45	DRS		830903
			(a) CKLST PT9a /003-048-017 PROT SUBM 2/14/83; CV's SUBM 7/13/82 WOLFF,STEVEN N CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			(b) CV # /PT 9b CV's FOR 3 ASSOC'S OF DR R GAMS (#34) UNDER PROT SUB 2/14/83				
L	Dec-02-83		AMENDMENT	83-46	DRS		830912
			(a) CV,CKLST,PROTOCOL PT9,10 /003-070-000 CV FOR DR JONES. HIS 3 ASSOCS' CV's WERE FILED 2/14/83 JONES,ROY CA-BREAST; DOSE RANGING ESCALATING DOSE -CARDIAC MEASUREMENTS				
L	Dec-12-83		CORRESPONDENCE UPDATED CARDIOTOX RPT TO SUPPORT REQUEST FOR 1A IND/NDA CLAS	83-47	DRS		830930
L	Dec-13-83		AMENDMENT	83-48	DRS		830932
			(a) CKLST,PROT PT9a,10 /003-072-001 CV SUBM 7/22/82 HENDERSON,I CRAIG CA-BREAST; SPECIAL-PK INFLUENCE OF HEPATIC FUNCTION				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(b) CV,CKLST,INVEST AGREE # /PT 9b DR ARLIN(#85) TO FOLLOW THE MULTI-CTR BR CA PROT SUB 2/14/83				
L	Dec-19-83		AMENDMENT	83-49	DRS		830943
			(a) CKLST # /PT 9 CL FOR DR QAZI(CV FILED 7/29/83);SUBBING FOR DR BENNETT,#111				
L	Jan-04-84		AMENDMENT	84-1	DRS		831034
			(a) CV # /PT 9 CVs FOR 2 ASSOCs OF DR BERTINO (#113) FOR PROT SUBM 11/11/83				
L	Jan-20-84		AMENDMENT	84-2	DRS		831068
			(a) INVEST BROCH # /PT 7 ADDENDUM TO 6/7/82 BROCHURE; RE: CARDIOTOXICITY				
			(b) CV(& ASSOCs),CKLST PT9 /003-048-019 PROTO SUBM 2/14/83 GEORGE,SEBASTIAN CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
F	Jan-23-84		CORRESPONDENCE REQUEST INFO ON POSSIBLE CAUSES & REMEDIES OF PRECIPITAION		GRP		831073
L	Jan-31-84	B Dec-21-83	CORRESPONDENCE SUMMARY/NOTES OF PRE-NDA DISCUSSION --FOR FDA REVIEW	84-3	DRS		831095
L	Feb-01-84		AMENDMENT	84-4	DRS		831106
			(a) CKLST /003-048-0 PROT SUBM 2/14/83; CV(& ASSOCs) SUBM 8/30/83 BERNARD,STEPHEN A CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE CL 232,315 ANTICANCER AGENT					
L	Feb-14-84		AMENDMENT	84-5	DRS		831144
			(a) CV,CKLST,INVEST AGREE # /PT 9a DR WEIDEN(#124) WILL FOLLOW MULTI-CTR BR CA PROT SUB 2/14/83				
L	Feb-21-84		AMENDMENT	84-6	DRS		831156
			(a) CKLST,PROT PT9a,10 /003-071-001 CV SUBM 1/25/83 CASE,DELVYN C LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			(b) CKLST,PROT PT9a,10 /003-074-001 CV SUBM 1/25/83 CASE,DELVYN C ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Feb-22-84		AMENDMENT	84-7	DRS		831160
			(a) DEAR INVESTIGATOR LETTER # /PT 7 WARNING TO READ LABELS CAREFULLY; OD(DEATHS) AT FOREIGN HOSP				
			(b) DEAR PHARMACIST LETTER # /PT 7 WARNING TO READ LABELS CAREFULLY; OD(DEATHS) AT FOREIGN HOSP				
			(c) CV,CKLST,PROTO PT9,10 /003-075-001 UPDATED CV ALBERTS,DAVID S CA-OV,COLON; DOSE RANGING PK OF IP ADMINISTRATION				
F	Feb-23-84	L Feb-23-84	ADVERTISING TORONTO TELECONFERENCE SEEN AS PROMOTION OF UNAPPROVED DRUG		ECM		831163
L	Feb-28-84		AMENDMENT	84-8	DRS		831166
			(a) CV,CKLST,INVEST AGREE # /PT 9a,c DR CONRAD(#125) WILL FOLLOW MULT-CTR BR CA PROT SUBM 2/14/83				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(b) CV,CKLST,INVEST AGREE # /PT 9b,c DR CHLEBOWSKI(#60;2nd STUDY) TO FOLL ADV BR CA PROT 12/13/83 (c) PROTOCOL AMNDMT TO MULTI-CTR CR CA PROT SUBM 2/14/83				
L	Mar-05-84		AMENDMENT	84-9	DRS		831266
			(a) CKLST PT9a /003-071-003 PROT SUBM 2/21/84; CV SUBM 10/10/83 ARLIN,ZALMEN A LYMPHOMA; vs m-BACOD m-BNCOD COMBO (b) CKLST PT9a /003-074-002 PROT SUBM 2/21/84; CV SUBM 10/10/83 ARLIN,ZALMEN A ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Mar-20-84		AMENDMENT	84-10	DRS		831289
			(a) CV,CKLST PT9a /003-071-002 DP 3-71 SUBM 2/21/84 MABRY,R JAMES LYMPHOMA; vs m-BACOD m-BNCOD COMBO (b) CV,CKLST PT9a /003-071-004 DP 3-71 SUBM 2/21/84 COHEN,RICHARD J LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
L	Mar-21-84		AMENDMENT	84-11	DRS		831290
			(a) CV # /PT 9 CV's FOR DRs ALVAREZ & RODRIGUES, DR ARLIN'S(#95) ASSISTANTS				
L	Mar-27-84		AMENDMENT	84-12	DRS		831300
			(a) CV,CKLST PT9a /003-048-024 DP 3-48 SUBM 2/14/83, AMENDED 2/28/84				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

PRESANT,CARY A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(b) CV,CKLST
PT9b /003-048-023
DP 3-48 SUBM 2/14/83, AMENDED 2/28/84
TRUMP,DONALD L
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(c) CV,CKLST
PT9b /003-048-025
DP 3-48 SUBM 2/14/83, AMENDED 2/28/84
DENEFRIO,JOHN M
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

L Mar-30-84 AMENDMENT 84-13 DRS 831302

(a) CKLST
PT9a /003-071-008
DP 3-71 SUBM 2/21/84; CV SUBM 1/25/83

(b) CV,CKLST
PT9b /003-071-005
DP 3-71 SUBM 2/21/84
DRESDNER,DAVID M
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(c) CV,CKLST
PT9b /003-071-007
DP 3-71 SUBM 2/21/84
BLUMING,AVRUM Z
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(d) CV,CKLST /003-074-0
DP 3-74 SUBM 2/21/84
DRESDNER,DAVID M
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

L Mar-30-84 F Jan-23-84 CORRESPONDENCE 84-14 GRP 831310
BUFFERED BISULFITE-FREE FORMULA'N HAS REPLACED
FORMER FORM'N

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Apr-02-84		AMENDMENT	84-15	DRS		831334
			(a) CKLST PT9a /003-071-006 MUL-CTR COMB REGIMEN PROT SUBM 2/21/84; CV SUBM 7/13/82 WOODCOCK,THOMAS M LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
L	Apr-09-84		AMENDMENT	84-16	DRS		831347
			(a) CKLST,CV-ASSOC(s) PT9a /003-048-026 PROT SUBM 2/14/83, AMENDED 2/28/84; CV SUBM 7/13/82 GRACE,WILLIAM R CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU (b) PROTOCOL # /PT 10 AMNDMT TO HEPATOMA PROT SUBM 6/11/82 (DR R CHLEBOWSKI #60)				
F	Apr-11-84	L Sep-14-83	NOT APPROVABLE REQUEST FOR 1A CLASSIFICATION DENIED		DRS		831351
L	Apr-16-84		AMENDMENT	84-17	DRS		831360
			(a) CV,CKLST PT9abc /003-071-012 DP 3-71 SUBM 2/21/84 ABBRUZZESE,JAMES L LYMPHOMA; vs m-BACOD m-BNCOD COMBO (b) CV,CKLST PT9abc /003-071-009 DP 3-71 SUBM 2/21/84 GOODMAN,GARY E LYMPHOMA; vs m-BACOD m-BNCOD COMBO (c) CV,CKLST PT9abc /003-071-013 DP 3-71 SUBM 2/21/84				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

HOLROYDE,CRISTPHER P
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(d) CKLST
PT9abc /003-071-010
DP 3-71 SUBM 2/21/84; STEIN'S (2nd STUDY) CV SUBM 12/8/82
STEIN,RICHARD S
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(e) CKLST
PT9abc /003-071-011
DP 3-71 SUBM 2/21/84; CV SUBM 7/13/82
WOLFF,STEVEN N
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

L Apr-19-84 AMENDMENT 84-18 DRS 831369

(a) CKLST
PT9a /003-072-003
3-72 SUBM 12/13/83; CV SUBM 7/13/82
WOODCOCK,THOMAS M
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION

L Apr-23-84 AMENDMENT 84-19 DRS 831370

(a) CV
CVs FOR 3 ASSTs OF DR D SPICER (#71)

L Apr-30-84 AMENDMENT 84-20 DRS 831379

(a) CKLST
PT9a /003-071-014
PROT SUBM 2/21/84; CV(& ASSOCs) SUBM 3/31/84
BENNETT,J/QAZI,RAMAN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(b) CV(& ASSOCs),CKLST
PT9b /003-074-004
PROT SUBM 2/21/84
GROPPE,CARL W
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

(c) CV-ASSOC(s)
PT9c /003-071-011
BERMAN,LEVINE,STREETER,RASSIGA

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

L May-02-84 AMENDMENT 84-21 DRS 831408

(a) CKLST
PT9 /003-071-016
PROT SUBM 2/21/84; CV SUBM 2/28/84
CONRAD,MARCEL E
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

L May-04-84 AMENDMENT 84-22 DRS 831415
DR KRAKOFF REPLACES DR BODEY(#100) AS PRINCIPLE INVESTIGATOR

(a) CV,CKLST
PT9 /003-041-001
KRAKOFF REPL BODEY AS PRIN INV; DP3-41 SUBM 6/7/82
KRAKOFF,I H
CA-BREAST
COMB W/ CYCLOPHOS, 5-FU X-OVER TO ADRIAMYCIN/VINBLASTINE

(b) CV(& ASSOCS),CKLST
PT9 /003-071-015
DP3-71 SUBM 2/21/84
SHAW,JOHN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(c) CV,CKLST
PT9 /003-047-001
KRAKOFF REPL BODEY AS PRIN INV; DP3-47 SUBM 2/9/83
KRAKOFF,I H

(d) INVESTIGATOR REPLACEMENT /003-041-0
BODEY REPLACED BY KRAKOFF
BODEY,GERALD P
CA-BREAST
COMB W/ CYCLOPHOS, 5-FU X-OVER TO ADRIAMYCIN/VINBLASTINE

(e) INVESTIGATOR REPLACEMENT /003-047-0
BODEY REPLACED BY KRAKOFF
BODEY,GERALD P

L May-22-84 AMENDMENT 84-23 DRS 831449

(a) CV(& ASSOCs),CKLST
PT9a,d /003-048-027
DP3-48 SUBM 2/14/83, AMND 2/29/84; UPDATED CV

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp	Event Due	ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

OISHI,NOBORU
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(b) CKLST
PT9b,c /003-071-018
DP3-71 SUBM 2/21/84; CV(& ASSOCs) SUBM 9/3/82
DOTY,GORDON L
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(c) CV,CKLST
PT9b,c /003-071-017
DP3-71 SUBM 2/21/84; ASSOCS' CVs SUBM 3/27/84
KENNEDY,PETER S
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(d) CV(& ASSOCs),CKLST
PT9b,c /003-071-019
DP3-71 SUBM 2/21/84
GABRIEL,DON A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(e) CV(&ASSOCs),CKLST
PT9b,c /003-071-012
DP3-71 SUBM 2/21/84
LEVINE,JAMES D
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(f) CV(& ASSOCs),CKLST
PT9b,c /003-071-020
DP3-71 SUBM 2/21/84
SCOTT,ROBERT B
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(g) INVESTIGATOR REPLACEMENT /003-071-0
ABBRUZZESE REPLACED BY LEVINE
ABBRUZZESE,JAMES L
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

L May-23-84 AMENDMENT 84-24 DRS 931463

(a) CV,CKLST
PT9a /003-000-000
DP3-48 SUBM 2/14/83,AMND 2/29/84; ONE
PT,COMPASSIONATE,OL

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp	Event Due	ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

SAMUELS,ARTHUR J
(b) CV,CKLST
PT9a /003-048-028
PROT SUBM 2/21/84
BENIGNO,BENEDICT R
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
(c) CV(& ASSOCs),CKLST
PT9a /003-071-021
DP3-71 SUBM 2/21/84
FASS,LEROY
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

L May-30-84 AMENDMENT 84-25 DRS 831481

(a) CV,CKLST
PT9 /003-074-005
MULTICTR COMBO REGIMEN ACUTE NONLYMPH LEUK PROT
SUBM 2/21/84
TRANUM,BILL L
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

L May-31-84 AMENDMENT 84-26 DRS 831480

(a) CKLST # /PT 9
CURRENTLY ACTIVE INVESTIGATORS
(b) PROGRESS RPT # /PT 10
ALBERTS,DAVID S
CA-OV,COLON; DOSE RANGING
PK OF IP ADMINISTRATION
ARLIN,ZALMEN A
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
ARLIN,ZALMEN A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
BERNARD,STEPHEN A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BERNARD,STEPHEN A
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			BERTINO,JOSEPH LEUKEMIA				
			CASE,DELVYN C ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			CASE,DELVYN C LYMPHOMA NON-HODGKIN'S				
			CASE,DELVYN C LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			DENEFRIO,JOHN M CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			DENEFRIO,JOHN M CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			GAMS,RICHARD A LYMPHOMA NON-HODGKIN'S				
			GOLOMB,HARVEY M LYMPHOMA NON-HODGKIN'S				
			GRACE,WILLIAM R CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			GRACE,WILLIAM R CA-BREAST; vs ADRIAMYCIN MULTI-CTR 2nd LINE PTS				
			HENDERSON,I CRAIG CA-BREAST; SPECIAL-PK INFLUENCE OF HEPATIC FUNCTION				
			HOLLAND,JAMES HOLLAND,JAMES F ALL COMBINED W/ VINCRISTINE & DEXAMETHASONE				
			HOLLAND,JAMES F LYMPHOMA COMBINED W/ VINCRISTINE & DEXAMETHASONE				
			JONES,ROY CA-BREAST; DOSE RANGING ESCALATING DOSE -CARDIAC MEASUREMENTS				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp	Event Due	ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT					

JONES,STEPHEN E
LYMPHOMA
NON-HODGKIN'S
KRAKOFF,IH /BODEY
KREMENTZ,EDWARD T
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
MORGAN,LEE ROY
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
MUGGIA,FRANCO
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PARKINSON,DAVID R
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PLOTKIN,DAVID
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PRESANT,CARY A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
RIVKIN,SAUL E
LYMPHOMA
NON-HODGKIN'S
SCHWARTZ,I ROBERT
LEUKEMIA

SEBASTIAN,GEORGE
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
SILVER,RICHARD T
LYMPHOMA
NON-HODGKIN'S
STUART,JOHN J
LYMPHOMA
NON-HODGKIN'S
TRUMP,DONALD L
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

VOGEL,CHARLES L
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WHITE,CHARLES F
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WOLFF,STEVEN N
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WOODCOCK,THOMAS M
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION
WOODCOCK,THOMAS M
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION

L Jun-06-84	AMENDMENT	84-27	ORS	831531		

(a) CKLST
PT9acd /003-071-023
DP3-71 SUBM 2/21/84; CV SUBM 10/7/82
BITRAN,JACOB
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(b) CKLST
PT9acd /003-071-025
DP3-71 SUBM 2/21/84; CV SUBM 9/10/82
BROUN,GORONWY O
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(c) CV,CKLST
PT9acd /003-071-024
DP3-71 SUBM 2/21/84
STONE,LAWRENCE A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(d) CV,CKLST
PT9acd /003-071-022
DP3-71 SUBM 2/21/84
VOYCE,GARY F
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(e) CV,CKLST,PROTO,INVES AGR
PT9b /003-074-006
ADDL STUDY BY DR GAMS; CV SUBM
1/4/83;PROT(3-74)SUBM 2/21/84

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Jun-14-84		AMENDMENT IN REFERENCE TO DR NEIDHART'S(#56) BREAST CA STUDY (3-43-1)	84-28	DJF		831543
			(a) CASE REPORT FORM GLOSSARY OF ABBREV'Ns/CODES(FOR CRFs) PREPARED BY OSU CA CTR				
L	Jun-15-84		AMENDMENT	84-29	DRS		831545
			(a) CKLST PT9a /003-071-014 CV SUBM 7/29/83; DP3-71 SUBM 2/21/84; QAZI CO-INV W/ BENNETT QAZI,RAMAN LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
L	Jun-19-84		AMENDMENT	84-30	DRS		831561
			(a) CKLST PT9acd /003-071-028 DP3-71 SUBM 2/21/84; CV(& ASSOCs) SUBM 1/4/83,6/6/84 GAMS,RICHARD A LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			(b) CKLST PT9acd /003-071-029 DP3-71 SUBM 2/21/84; CV(& ASSOCs) SUBM 6/24/83 WIERNIK,PETER H LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			(c) CV(& ASSOCs),CKLST PT9acd /003-071-026 (3-71) SUBM 2/21/84 HEIM,WILLIAM J LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			(d) CV,CKLST PT9acd /003-071-027 (3-71) SUBM 2/21/84 WACHI,DENNIS H LYMPHOMA; vs m-BACOD m-BNCOD COMBO				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(e) CKLST
PT9acd /003-072-004
DP3-72 SUBM 12/13/83; CV(& ASSOCs) SUBM 10/10/83
ARLIN,ZALMEN A
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION

(f) CV(& ASSOCs),CKLST
PT9acd /003-074-007
DP3-74 SUBM 2/21/84
ABRAMSON,NEIL
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

(g) CV,CKLST
PT9acd /003-074-006
DP3-74 SUBM 2/21/84
VILLA,LUIS
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

(h) CKLST
PT9acd /003-074-008
DP3-74 SUBM 2/21/84; CV(&ASSOCs) SUBM 6/24/83
WIERNIK,PETER H
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

L Jun-22-84 AMENDMENT 84-31 DRS 831566

(a) CV,CKLST
PT9a /003-074-009
DP3-74 SUBM 2/21/84
HICKS,WILLIAM J
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

L Jul-02-84 AMENDMENT 84-32 DRS 831667

(a) CKLST
PT9a /003-071-030
PROT 3-71 SUBM 2/21/84; CV(& ASSOCs) SUBM 7/13/82, 2/3/83
SILVER,RICHARD T
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(b) CV,CKLST
PT9b /003-043-001
ROACH REPL NEIDHART(#56) AS PRIN INV IN DP 3-43
SUBM 8/24/82

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

ROACH,RALPH W
(c) PROTOCOL /003-000-0
QAZI FOLLOWING (BUT NOT PART OF) DP3-48 SUBM 2/14/83
QAZI,RAMAN

L Jul-12-84 AMENDMENT 84-33 DRS 831691

(a) CKLST
PT9a /003-071-031
PROT 3-71 SUBM 2/21/84; CV SUBM 3/7/83
WHITE,CHARLES F
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

(b) CKLST
PT9b /003-040-009
HESKETH REPL LOPEZ AS PRN INV; DP3-40 SUB 7/13/82;CV-4/30/84
HESKETH,PAUL /LOPEZ
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS

(c) CV,CKLST
PT9b /003-048-029
PROT 3-48 SUBM 2/14/83, AMENDED 2/28/84
PORTLOCK,CAROL S
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

L Jul-13-84 AMENDMENT 84-34 DRS 831692

(a) CV # /PT 9
CVs FOR 3 ASSTs UNDER DR GRACE (#63; 3-40-3 -SUBM 7/13/82)

L Jul-20-84 AMENDMENT 84-35 DRS 831702

(a) CV # /PT 9
CVs FOR 5 ASSTs TO TRUMP(#128;3-48-23); 3-48 SUBM 2/14/83

L Jul-23-84 AMENDMENT 84-36 DJF 831711
DER FROM DR DAO'S TRIAL (3-40-16) -MULTI-CTR BR CA PROT 3-40

(a) DRUG EXPER RPT # /PT 10
PT #3018 (AGE:30yrs) AMENORRHEA, HOT FLASHES

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Jul-26-84		AMENDMENT	84-37	DJF		831705
			(a) CKLST PT9a /003-071-033 PROT 3-71 SUBM 2/21/84; ARMENTROUT'S CV SUBM 9/10/82 ARMENTROUT,STEVEN LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			(b) CV,CKLST PT9a /003-071-032 PROT 3-71 SUBM 2/21/84; JAFFREY,IRA S LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
			(c) CV-ASSOC(s) PT9c /003-071-028 11 ASSOCs TO GAMS (PROT SUBM 2/21/84)				
L	Jul-27-84	L Jul-13-84	CORRESPONDENCE 7/13/84 COVER LTR SHOULD HAVE READ 16,332 & NOT 17,560		DJF		831742
L	Jul-30-84		AMENDMENT	84-38	DJF		831740
			(a) CV,CKLST PT9 /003-074-010 DP3-74 SUBM 2/21/84 WEINTRAUB,LEWIS R ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Aug-06-84		AMENDMENT	84-39	DJF		831756
			(a) CKLST PT9a /003-074-012 DP3-74 SUBM 2/21/84; CV(& ASSOCs) SUBM 9/3/82 DOTY,GORDON L ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			(b) CV,CKLST PT9b /003-071-034 DP3-71 SUBM 2/21/84 DOSIK,MICHAEL H LYMPHOMA; vs m-BACOD m-BNCOD COMBO				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Aug-07-84		AMENDMENT	84-40	DJF		831763
		(a)	CKLST PT9a /003-071-023 DESSER (CV-10/7/82) REPLACES BITRAN AS PR INV FOR 3-71-23 BITRAN,JACOB LYMPHOMA; vs m-BACOD m-BNCOD COMBO DESSER,R K /BITRAN LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
		(b)	CV-ASSOC(s) # /PT 9b 4 ASSOCs OF DR H GOLOMB FOR 2 BR CA STUDIES -3-40-21,3-48-21				
L	Aug-14-84		AMENDMENT	84-41	DJF		831774
		(a)	CV,CKLST,PROTO PT9,10 /003-069-001 UPDATED CV MOORE,JOSEPH O CA-LUNG WITH CIS-PLATINUM IN ADENO CA OR LARGE CELL CA				
L	Aug-15-84		MEETING REQUEST MTG SEPT 24-26: ACUTE LEUKEMIA & NON-HODGKIN'S LYMPH	84-42	DJF		831777
L	Aug-16-84		AMENDMENT	84-43	DJF		831812
		(a)	CKLST PT9a /003-074-011 3-74 SUBM 2/21/84; CV(& 13 ASSOCs) SUBM 1/4/83, 5/6,7/26/84 GAMS,RICHARD A ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
		(b)	CV-ASSOC(s) PT9b /003-048-008 FOR 2 ASSTs TO DR BRODOVSKY (#109 -3/7/83) IN STUDY 3-48-8				
		(c)	CV-ASSOC(s) PT9b /003-048-007 1 ASST TO DR HOLROYDE (#134 -4/16/84) IN STUDY 3-71-13				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(d) CV-ASSOC(s) PT9c /003-048-007				
			(d) CV-ASSOC(s) PT9c /003-071-031				
			(e) CV-ASSOC(s) PT9d /003-048-023 FOR 8 ASSTs				
L	Aug-23-84		AMENDMENT	84-44	DJF		831825
			(a) DEAR INVESTIGATOR LETTER # /PT 7 TO ALL ACTIVE INVs: AMENORRHEA IN PTS BEING TREATED W/ MITOX				
L	Aug-24-84		AMENDMENT	84-45	DJF		831829
			(a) ALL INVSTGTRS (EXCEPT HEIM) WILL FOLLOW 3-74 SUBM 2/21/84				
			(b) CKLST PT9b /003-074-016 DP3-74 SUBM 2/21/84; CV(& ASSOCs) SUBM 5/22/84,8/30/83 GABRIEL,DON A ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			(c) CKLST PT9a /003-074-017 DP3-74 SUBM 2/21/84; CV(& ASSOCs) SUBM 7/13/82,2/3/83 SILVER,RICHARD T ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			(d) CV(& ASSOCs),CKLST PT9c /003-074-015 DP3-74 SUBM 2/21/84 DOSIK,HARVEY ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			(e) CV(& ASSOCs),CKLST PT9c /003-074-014 DP3-74 SUBM 2/21/84 KLOSS,ROBERT A ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(f) CV(& ASSOCs),CKLST
PT9c /003-074-013
DP3-74 SUBM 2/21/84
ROBINSON,WILLIAM
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

(g) CV-ASSOC(s)
PT9d /003-071-026
FOR 1 ASST TO DR HEIM (#150 -6/19/84) IN STUDY
3-71-26

L Aug-30-84 AMENDMENT 84-46 DJF 831835

(a) CV-ASSOC(s) # /PT 9
1 ASST TO DR WHITE(#116 -8/17/83); PROT 3-48 SUBM
2/14/83

(b) DRUG EXPER RPT # /PT 10
STUDY 3-48-8 (PT: EP #4102): HYPOTENSION

L Sep-05-84 AMENDMENT 84-47 DJF 831852

(a) CV(& ASSOCs),CKLST
PT9a /003-074-018
DP3-74 SUBM 2/21/84; CV FOR 4 ASSOCs
SCHADE,STANLEY G
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

(b) CV-ASSOC(s) # /PT 9b
1 ASST TO TRUMP(#128,3-48-23,3/27/84); DP3-48 SUBM
2/14/83

L Sep-06-84 AMENDMENT 84-48 DJF 831853

(a) CKLST
PT9a /003-069-002
DP 3-69 SUBM 8/14/84; CV(& ASSOCs) SUBM 5/22/84 &
8/30/83
BERNARD,STEPHEN A
CA-LUNG
WITH CIS-PLATINUM IN ADENO CA OR LARGE CELL CA

(b) CV-ASSOC(s)
PT9b /003-071-014
BRENNAN,OLSON,ROWE

(c) CV-ASSOC(s)
PT9c /003-074-007
JADEJA,MAHAJAN

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Sep-12-84		AMENDMENT	84-49	DJF		831861
		(a)	CV(& ASSOCs),CKLST PT9 /003-074-019 DP3-74 SUBM 2/21/84 KARP,DANIEL D ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Sep-19-84		AMENDMENT	84-51	DJF		831878
		(a)	CKLST PT9a /003-071-035 (3-71-35); CV(& ASSOC) SUBM 1/20/84; DP3-71 SUBM 2/21/84 GEORGE,SEBASTIAN LYMPHOMA; vs m-BACOD m-BNCOD COMBO				
		(b)	CV-ASSOC(s) # /PT 9b 2 ASSOCs OF DR BITRAN(#87,3-40-23-10/7/82);3-40 SUBM 7/13/82				
		(c)	CV-ASSOC(s) # /PT 9c 7 ASSOCs OF PORTLOCK(#156,3-48-29-7/12/84);3-48 SUBM 2/14/83				
		(d)	DRUG EXPER RPT # /PT 10 PT#1006,3-74-2: DEATH -3hrs AFTER MITO + Ara-C ADMINISTERED				
L	Sep-20-84		AMENDMENT	84-52	DJF		831881
		(a)	CV-ASSOC(s) # /PT 9 4 ASSOCs TO TRUMP(#128,3-48-23 3/27/84); DP3-48 SUBM 2/14/83				
L	Sep-26-84		AMENDMENT	84-53	DJF		850125
		(a)	CKLST,CV-ASSOC(s) PT9a,b /003-040-021 REPL GOLOMB(#79) AS PR INV IN 3-40 SUBM 7/13/82,AMND 1/10/83 BITRAN,JACOB /GOLOMB CA-BREAST; vs ADRIAMYCIN MULTI-CTR 2nd LINE PTS GOLOMB,HARVEY M CA-BREAST; vs ADRIAMYCIN MULTI-CTR 2nd LINE PTS				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(b) CKLST,CV-ASSOC(s) PT9a,b /003-048-010 BITRAN REPL GOLOMB AS PR INV IN 3-48 SUBM 2/14/83, A 2/28/84 BITRAN,JACOB /GOLOMB CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU BITRAN,JACOB /GOLOMB CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU GOLOMB,HARVEY M CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			(c) CV-ASSOC(s) PT9b /003-046-007 3-46 SUBM 12/8/82, AMND 6/21/83; BITRAN'S CV SUBM 10/7/82				
			(d) CV-ASSOC(s) PT9c /003-071-034 FOR 12 ASSTs TO DR M DOSIK(#159-8/16/84); 3-71 SUBM 2/21/84				
			(e) PROTOCOL AMENDMENT PT10a /003-065-000 A#2 -PROT ORIG SUBM 7/29/83, AMND 8/26/83				
			(f) PROTOCOL AMENDMENT PT10b /003-074-000 A#1 -PROT SUBM 2/21/84				
L	Oct-04-84		AMENDMENT	84-54	DJF		831938
			(a) CV(& ASSOCs),CKLST PT9a /003-074-020 3-74 SUBM 2/21/84, AMENDED 9/26/84 WEAVER,ZEBULON III ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Oct-17-84		AMENDMENT	84-55	DJF		831935
			(a) CV-ASSOC(s) PT9 /003-071-001 1 ASST TO CASE (#98,3-71-1 SUBM 2/21/84)				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE CL 232,315 ANTICANCER AGENT					
L	Oct-19-84		AMENDMENT	84-56	DJF		831939
		(a)	CV-ASSOC(s) # /PT 9 4 ASSTS TO ARLIN (#85,3-44-13,10/1/82); 3-44 SUBM 9/10/82				
L	Oct-24-84		AMENDMENT	84-58	DJF		831942
		(a)	CKLST & PROTOCOL PT9 /003-074-021 CV SUBM 9/10/82 ARMENTROUT,STEVEN ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Oct-24-84		CORRESPONDENCE COPY OF 9/26 MINUTES: EVAL'N OF MITO IN PTS W/ LEUK/LYMPHOMA	84-57	DJF		831941
L	Oct-29-84		AMENDMENT	84-59	DJF		831962
		(a)	CKLST & PROTOCOL PT9,10 /003-000-000 CV SUBM 12/3/82 BERNHARDT,BERNARD				
L	Nov-05-84		AMENDMENT	84-60	DJF		832033
		(a)	CV-ASSOC(s) PT9 /003-046-002 7 ASSTs TO PETERSON (#94-12/8/82); PROT SUBM 12/8/82				
L	Nov-07-84		AMENDMENT	84-61	DJF		832036
		(a)	CV-ASSOC(s) PT9a /003-071-013 2 ASSTs TO HOLROYDE(#134-4/16/84); DP3-71 SUBM 2/21/84				
		(b)	CV-ASSOC(s) PT9b /003-000-000 PHILLIPS ASST'g BERNHARDT IN PROT SUBM 10/29/84,1PT-COMPASSN				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE CL 232,315 ANTICANCER AGENT					
L	Nov-09-84	L Oct-24-84	CORRESPONDENCE	84-62	DJF		832038
			(a) PUBLISHED RPTS SWOG PAPER (CANCER'79): ADRIAMYCIN'S CONTRIBUTION DIFF LYMPH				
L	Nov-13-84		AMENDMENT	84-63	DJF		832040
			(a) CKLST PT9 /003-069-003 DP3-69 SUBM 8/14/84; CV(& ASSOCs) SUBM 4/9/84,7/13/82 SARG,MICHAEL J CA-LUNG WITH CIS-PLATINUM IN ADENO CA OR LARGE CELL CA				
L	Nov-14-84		AMENDMENT	84-64	DJF		832042
			(a) CV-ASSOC(s) PT9a /003-048-020 ASST TO BERNARD(#117-2/1/84); DP3-48 SUBM 2/14/83,A-2/28/84				
			(b) CV-ASSOC(s) PT9b /003-074-015 2 ASSTs TO DOSIK(#163-8/24/84); DP3-74 SUBM 2/21/84,A9/26/84				
L	Nov-27-84		AMENDMENT	84-65	DJF		832067
			(a) PROTOCOL AMENDMENT PT10 /003-046-000 AMNDMT 2 (DP3-46 ORIG SUBM 12/8/82, FIRST AMND' 6/21/83)				
L	Nov-30-84		AMENDMENT	84-67	DJF		832069
			(a) CV,CKLST PT9 /003-000-000 SPAULDING FOLLOWING (BUT NOT PART OF) DP3-40 SUBM 7/13/82 SPAULDING,MONICA B				
L	Dec-05-84		AMENDMENT	84-68	DJF		832103
			(a) CV-ASSOC(s) PT9 /003-071-031 ASST TO WHITE (#116,7/12/84); DP3-71 SUBM 2/21/84				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Dec-20-84		AMENDMENT	84-69	GRP	F	832144
			IN SUPPORT OF PRESERV EFFICACY -VIALS AS MULT-DOSE CONTAINER				
			(a) PRESERVATIVE EFFICACY # /PT 5 AT 30 MINS; 1,7,14,21,28 DAYS (EXHIBIT #1)				
			(b) PRESERVATIVE EFFICACY # /PT 5 AT 6,24,48 HRS & 7,14,21,28 DAYS (EXHIBIT #2)				
			(c) ANALYSES # /PT 5 MULT-USE EVAL'N: REPEATED EXTRACTIONS FROM A SINGLE VIAL 30d				
			(d) MONOGRAPH # 15530 /PT 5 GENERAL MTD: ANTIMICROBIAL PRESERVATIVES EFFECTIVENESS				
L	Jan-02-85		AMENDMENT	85-1	DJF		832126
			(a) DRUG EXPER RPT PT10 /003-074-007 PT#2019 DEATH: FIBRILLATION ATRIAL				
L	Jan-18-85		AMENDMENT	85-2	DJF		850033
			(a) CKLST, PROT PT9a,10a /003-076-001 CV SUBM 10/4/84 WEAVER,ZEBULON III CA-SOLID; COMPASSIONATE				
			(b) CV,CKLST,PROTO PT9b,10b /003-077-001 COOPER,MILES R LEUKEMIA; COMPASSIONATE				
F	Jan-22-85	L Oct-24-84	CORRESPONDENCE		DJF		850274
			IF MITO ADDS TO RESULTS OF H-D CYTARAB (ANLL) EFICCACY SHOWN				
			(a) EFFICACY(NOD LYMPH): IMPROVE QUALITY OF LIFE;SURVIV DATA REQ				
L	Feb-19-85		AMENDMENT	85-3	DJF		850120

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(a) CKLST
PT9a /003-000-000
DP3-65 SUBM 7/29/83, AMENDED 8/26/83,9/26/84. CV SUB 2/14/83
HOLLAND,JAMES

(b) CV,CKLST
PT9b /003-076-002
DP3-76 SUBM 1/18/85
GRILLO,JAMES
CA-SOLID; COMPASSIONATE

(c) PROTOCOL AMENDMENT
PT10 /003-075-001
A#1: PTS OVER 70yrs WILL BE ADMITTED; DP3-75 SUBM 2/22/84

L Feb-26-85 AMENDMENT 85-4 DJF 850142

(a) CV-ASSOC(s)
PT9 /003-071-015
ASST TO SHAW (#138 -5/4/84); DP3-71 SUBM 2/21/84

(b) DRUG EXPERIENCE RPT # /PT 10
(U.K. STUDY 3-563-1, PT# 1/G.N.) INTESTINAL PERFORATION

L Mar-01-85 AMENDMENT 85-6 DJF 850189

(a) CV,CKLST
PT9a /003-076-003
PROT SUBM 1/18/85
LOWENBRAUN,STANLEY
CA-SOLID; COMPASSIONATE

(b) CV(& ASSOCs),CKLST
PT9b /003-076-004
PROT SUBM 1/18/85
SCHER,NANCY
CA-SOLID; COMPASSIONATE

(c) CKLST
PT10c /003-076-005
PROT SUBM 1/18/85; CV SUBM 7/26/84 UNDER PROT 3-71-32
JAFFREY,IRA S
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(d) CKLST
PT10d /003-076-006
PROT SUBM 1/18/85; CV SUBM 3/27/84 UNDER PROT 3-48-5
DENEFRIO,JOHN M
CA-SOLID; COMPASSIONATE

(e) /003-076-0
DR Z WEAVER(#166) WILL BE TREATING AN ADDL PATIENT

(f) /003-077-0
DR COOPER(#170) WILL BE TREATING AN ADDL PATIENT

L Mar-08-85 AMENDMENT 85-8 DJF 850179

(a) DRUG EXPERIENCE RPT # /PT 10
(CANADA) EXTRAVASATION; SWELLING, BLISTERING, WEAKNESS -HAND

L Mar-15-85 AMENDMENT 85-8 DJF 850214

(a) CV(& ASSOCs),CKLST
PT9 /003-077-002
PROT SUBM 1/18/85
McFARLAND,JAMES A
LEUKEMIA; COMPASSIONATE

L Mar-25-85 AMENDMENT 85-9 DJF 850239

(a) CV(& ASSOCs),CKLST
PT9a /003-076-007
PROT SUBM 1/18/85
HORVATH,WILLIAM L
CA-SOLID; COMPASSIONATE

(b) CV-ASSOC(s)
PT9b /003-074-015
2 ASSTS TO DOSIK; PROT SUBM 2/21/84

L Apr-10-85 AMENDMENT 85-10 DJF 850310

(a) CV,CKLST
PT9 /003-076-008
PROT SUBM 1/18/85
STRUM,STEPHEN B
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Apr-15-85		AMENDMENT	85-11	DJF		850313
		(a)	CKLST,PROT,CV-ASSOC(s) PT9 /003-074-022 PROT SUBM 2/21/84, AMND 9/26/84; CV SUBM 8/14/84 MOORE,JOSEPH D ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
		(b)	DRUG EXPERIENCE RPT PT10 /003-070-001 PT #25: TISSUE NECROSIS				
L	Apr-23-85		AMENDMENT	85-12	DJF		850348
		(a)	CV(& ASSOCs),CKLST PT9 /003-076-009 PROT SUBM 1/18/85 GOTTLEIB,ROBERT J CA-SOLID; COMPASSIONATE				
		(b)	/003-071-0 BERKOWITZ (CV SUBM 8/24/84) ADDED AS ASST INVESTIGATOR				
L	May-10-85		AMENDMENT	85-13	DJF		850459
		(a)	CV,CKLST PT9 /003-076-010 PROT SUBM 1/18/85 ROBERTS,JOHN CA-SOLID; COMPASSIONATE				
		(b)	CV(& ASSOCs),CKLST,PROT PT9,10 /003-079-001 SRIDHAR,KASI CA-HEAD & NECK				
		(c)	CV(& ASSOCs),CKLST,PROT PT9,10 /003-080-001 KELSEN,DAVID CA-STOMACH				
L	May-14-85		AMENDMENT	85-14	DJF		850468

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(a) CV,CKLST
PT9a /003-076-011
PROT SUBM 1/18/85
KOO,VICTOR S
CA-SOLID; COMPASSIONATE

(b) CV(& ASSOCs),CKLST
PT9b /003-077-004
PROT SUBM 1/18/85
FORTE,FRANCIS A
LEUKEMIA; COMPASSIONATE

L May-15-85 AMENDMENT 85-15 DJF 850469

(a) CV(& ASSOCs),CKLST
PT9 /003-077-003
PROT SUBM 1/18/85
ALBALA,MAURICE
LEUKEMIA; COMPASSIONATE

L May-21-85 AMENDMENT 85-16 DJF 850473

(a) CKLST
PT9 /003-076-012
PROT SUBM 1/18/85; CV(& ASSOCs) SUBM 5/14/85
FORTE,FRANCIS A
CA-SOLID; COMPASSIONATE

L May-24-85 AMENDMENT 85-17 DJF 850440

(a) CKLST # /PT 9
CURRENTLY ACTIVE INVESTIGATORS (AS OF 4/15/85)
(b) PROGRESS RPT # /PT 10
ABRAMSON,NEIL
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
ALBERTS,DAVID S
CA-OV,COLON; DOSE RANGING
PK OF IP ADMINISTRATION
ALLEGRA/WOODCOCK
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
AMARE
LEUKEMIA

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

ARLIN,ZALMEN A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
ARLIN,ZALMEN A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
ARLIN,ZALMEN A
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
ARLIN,ZALMEN A
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION
ARLIN,ZALMEN A
LEUKEMIA

ARLIN,ZALMEN A
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
ARMENTROUT,STEVEN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
ARMENTROUT,STEVEN
LEUKEMIA

ARMENTROUT,STEVEN
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
BENIGNO,BENEDICT R
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BENNETT,J/QAZI,RAMAN
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BENNETT,J/QAZI,RAMAN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
BERNARD,STEPHEN A
CA-LUNG
WITH CIS-PLATINUM IN ADENO CA OR LARGE CELL CA
BERNARD,STEPHEN A
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
BERNARD,STEPHEN A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

BERNHARDT,BERNARD
BITRAN,JACOB /GOLOMB
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
BLOCK
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
BLUMING,AVRUM Z
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
BRODORSKY
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BROUN,GORONWY O
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
BROUN,GORONWY O
LEUKEMIA

BYRNE
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
CASE,DELVYN C
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
CASE,DELVYN C
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
CASE,DELVYN C
LYMPHOMA
NON-HODGKIN'S
CASSILETH
LEUKEMIA

CHLEBOWSKI
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION
CHLEBOWSKI
HEPATOMA

COHEN,RICHARD J
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
CONRAD,MARCEL E
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

CONRAD,MARCEL E
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
COOPER,MILES R
LEUKEMIA; COMPASSIONATE

COSTANZI,JOHN J
LYMPHOMA
NON-HODGKIN'S
DAO
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
DENEFRIO,JOHN M
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
DENEFRIO,JOHN M
CA-SOLID; COMPASSIONATE

DESAI
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
DESSER,R K
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
DOROSHOW
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
DOSIK,HARVEY
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
DOSIK,MICHAEL H
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
DOTY,GORDON L
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
DOTY,GORDON L
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
DOTY,GORDON L
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
DRESDNER,DAVID M
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

DRESDNER,DAVID M
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
DUGAN
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
ERSLEV,ALLAN J
LEUKEMIA

ERSLEV,ALLAN J
LYMPHOMA
NON-HODGKIN'S
FASS,LEROY
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GABRIEL,DON A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GABRIEL,DON A
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
GAMS,RICHARD A
LYMPHOMA
NON-HODGKIN'S
GAMS,RICHARD A
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
GAMS,RICHARD A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GAMS,RICHARD A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
GAMS,RICHARD A
LEUKEMIA

GEORGE,SEBASTIAN
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
GEORGE,SEBASTIAN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GOLOMB,HARVEY M
LYMPHOMA
NON-HODGKIN'S

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

GOODMAN,GARY E
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GRACE,WILLIAM R
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
GRACE,WILLIAM R
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
GRILLO,JAMES
CA-SOLID; COMPASSIONATE

GROPPE,CARL W
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
HEIM,WILLIAM J
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
HENDERSON,I CRAIG
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION
HESKETH,PAUL
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
HICKS,WILLIAM J
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
HOLLAND,JAMES
LEUKEMIA

HOLLAND,JAMES F
HOLLAND,JAMES F
ALL
COMBINED w/ VINCRISTINE & DEXAMETHASONE
HOLLAND,JAMES F
LYMPHOMA
COMBINED w/ VINCRISTINE & DEXAMETHASONE
HOLROYDE,CRISTPHER P
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
HORVATH,WILLIAM L
CA-SOLID; COMPASSIONATE

JAFFREY,IRA S
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

JAFFREY,IRA S
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
JONES,ROY
CA-BREAST; DOSE RANGING
ESCALATING DOSE -CARDIAC MEASUREMENTS
JONES,STEPHEN E
LYMPHOMA
NON-HODGKIN'S
KARP,DANIEL D
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
KENNEDY,PETER S
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
KLOSS,ROBERT A
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
KRAKOFF,I H
KRAKOFF,I H
CA-BREAST
COMB w/ CYCLOPHOS, 5-FU X-OVER TO
ADRIAMYCIN/VINBLASTINE
KREMENTZ,EDWARD T
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
KREMENTZ,EDWARD T
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
LAWSON
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
LEVICK
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
LEVINE,JAMES D
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
LOWENBRAUN,STANLEY
CA-SOLID; COMPASSIONATE

MABRY,R JAMES
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
MOORE,JOSEPH O
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

MOORE,JOSEPH O
CA-LUNG
WITH CIS-PLATINUM IN ADENO CA OR LARGE CELL CA
MOORE,JOSEPH O
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
MOORE,JOSEPH O
LEUKEMIA

MORGAN,LEE ROY
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
MUGGIA,FRANCO
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
MUSS
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
McFARLAND,JAMES A
LEUKEMIA; COMPASSIONATE

OISHI,NOBORU
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PETERSEN
LYMPHOMA
NON-HODGKIN'S
PLOTKIN,DAVID
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PORTLOCK,CAROL S
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PRESANT,CARY A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
QAZI,RAMAN
RIVKIN,SAUL E
LYMPHOMA
NON-HODGKIN'S

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

ROACH,RALPH W
ROBINSON,WILLIAM
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
POSS
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
SAMUELS,ARTHUR J
SARG,MICHAEL J
CA-LUNG
WITH CIS-PLATINUM IN ADENO CA OR LARGE CELL CA
SARTIANO,GEORGE P
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
SARTIANO,GEORGE P
LEUKEMIA

SCHADE,STANLEY G
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
SCHER,NANCY
CA-SOLID; COMPASSIONATE

SCHWARTZ,I ROBERT
LEUKEMIA

SCOTT,ROBERT B
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
SEBASTIAN,GEORGE
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
SHAW,JOHN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
SILVER,RICHARD T
LYMPHOMA
NON-HODGKIN'S
SILVER,RICHARD T
LEUKEMIA

SILVER,RICHARD T
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
SILVER,RICHARD T
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			SPAULDING,MONICA B				
			SPICER				
			CA-BREAST; vs ADRIAMYCIN				
			MULTI-CTR 2nd LINE PTS				
			STEIN,RICHARD S				
			LYMPHOMA				
			NON-HODGKIN'S				
			STEIN,RICHARD S				
			LYMPHOMA; vs m-BACOD				
			m-BNCOD COMBO				
			STONE,LAWRENCE A				
			LYMPHOMA; vs m-BACOD				
			m-BNCOD COMBO				
			STRUM,STEPHEN B				
			CA-SOLID; COMPASSIONATE				
			STUART,JOHN J				
			LYMPHOMA				
			NON-HODGKIN'S				
			STUART,JOHN J				
			LYMPHOMA; vs m-BACOD				
			m-BNCOD COMBO				
			TRANUM,BILL L				
			ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)				
			IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			TRUMP,DONALD L				
			CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)				
			CYCLOPHOSPHAMIDE-N-5FU vs				
			CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			VILLA,LUIS				
			ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)				
			IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
			VOGEL,CHARLES L				
			CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)				
			CYCLOPHOSPHAMIDE-N-5FU vs				
			CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
			VOLBERDING				
			CA-BREAST; vs ADRIAMYCIN				
			MULTI-CTR 2nd LINE PTS				
			VOYCE,GARY F				
			LYMPHOMA; vs m-BACOD				
			m-BNCOD COMBO				
			WACHI,DENNIS H				
			LYMPHOMA; vs m-BACOD				
			m-BNCOD COMBO				
			WEAVER,ZEBULON III				
			ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)				
			IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

WEAVER,ZEBULON III
CA-SOLID; COMPASSIONATE

WEIDEN
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WEINTRAUB,LEWIS R
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
WHITE
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
WHITE,CHARLES F
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
WHITE,CHARLES F
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WIERNIK,PETER H
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
WIERNIK,PETER H
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C)
IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
WIERNIK,PETER H
LEUKEMIA

WOLFF,STEVEN N
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
WOLFF,STEVEN N
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WOLFF,STEVEN N
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
WOODCOCK,THOMAS M
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION
WOODCOCK,THOMAS M
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
(c) TOXICOLOGY STUDIES # /PT 10
APPENDED CARDIOTOXICITY REPORT

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	May-29-85		AMENDMENT	85-18	DJF		850512
			(a) CV(& ASSOCs),CKLST PT9a /003-076-014 COMPASSIONATE PROT (SOLID TUMORS) SUBM 1/18/85 NELSON,ERIC C CA-SOLID; COMPASSIONATE				
			(b) CV(& ASSOCs),CKLST PT9b /003-077-005 COMPASSIONATE PROT (LEUKEMIA) SUBM 1/18/85				
L	May-30-85		AMENDMENT	85-19	DJF		850511
			(a) CV-ASSOC(s) PT9 /003-074-015 CV FOR DR S ROTHENBERG; PROT SUBM 2/21/84, AMENDED 9/24/84				
L	Jun-03-85		AMENDMENT	85-20	DJF		850533
			(a) CV,CKLST PT9 /003-046-003 MILLER REPLACES JONES AS PRINC INVEST; PROT SUBM 12/8/82 JONES,STEPHEN E LYMPHOMA NON-HODGKIN'S MILLER,THOMAS /JONES LYMPHOMA NON-HODGKIN'S				
L	Jun-25-85		AMENDMENT	85-21	DJF		850599
			(a) CV-ASSOC(s) PT9a /003-048-028 7 ASSOCS; PROT SUBM 2/21/84				
			(b) CV,CKLST PT9b /003-076-015 COMPASSIONATE PROT SUBM 1/18/85 ARENA,PAUL CA-SOLID; COMPASSIONATE				
			(c) CV,CKLST PT9b /003-076-017 COMPASSIONATE PROT SUBM 1/18/85				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			BUDD,THOMAS G CA-SOLID; COMPASSIONATE				
			(d) CV(& ASSOCs),CKLST PT9c /003-077-006 COMPASSIONATE PROT SUBM 1/18/85 SAUNDERS,DARRELL F LEUKEMIA; COMPASSIONATE				
			(e) CV(& ASSOCs),CKLST PT9d /003-044-000 (ONE PT) FOLLOWING MITO TRTMT SECT OF LEUK PROT SUBM 9/10/82 ALGAZY,KENNETH M LEUKEMIA				
L	Jun-26-85		AMENDMENT	85-22	DJF		850606
			(a) CV(& ASSOCs),CKLST,PROT PT9,10 /003-079-002 ERVIN,THOMAS CA-HEAD & NECK				
L	Jul-08-85		AMENDMENT	85-23	DJF		850659
			(a) CV(& ASSOCs),CKLST PT9 /003-080-002 PROT SUBM 5/10/85 BENEDETTO,PASQUALE CA-STOMACH				
L	Jul-31-85		AMENDMENT	85-24	DJF		850700
			(a) CV-ASSOC(s) PT9 /003-079-002 2 ASSOCs TO ERVIN (#187); PROT SUBM 6/26/85				
			(b) PROTOCOL AMENDMENT PT10 /003-072-000 A#1: OPTIONAL TESTS; PROT SUBM 12/13/83				
			(c) PROTOCOL AMENDMENT PT10 /003-072-000 A#2: MISCELLANEOUS CHANGES; PROT SUBM 12/13/83				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Aug-02-85		AMENDMENT	85-25	DJF		850769
		(a)	CV(& ASSOCs),CKLST PT9ab /003-072-005 UPDATED CVs (PROT SUBM 12/13/83, AMENDED I&II 7/31/85) CASE,DELVYN C CA-BREAST; SPECIAL-PK INFLUENCE OF HEPATIC FUNCTION				
L	Aug-06-85		AMENDMENT	85-26	DJF		850753
		(a)	PROTOCOL AMENDMENT PT10a /003-046-010 A #2A: MUGA SCAN OR ECHO ALLOWED (PROT SUBM 12/8/82)				
		(b)	PROTOCOL AMENDMENT PT10b /003-071-030 A #1A: MUGA SCAN OR ECHO ALLOWED (PROT SUBM 2/21/84)				
L	Aug-07-85		AMENDMENT	85-27	DJF		850755
		(a)	PROTOCOL AMENDMENT PT10 /003-074-000 A#2: NO CNS LEUK AT BASELINE (PROT SUBM 2/21/84)				
L	Aug-12-85		AMENDMENT	85-28	DJF		850791
		(a)	CV,CKLST PT9 /003-076-019 PROT SUBM 1/18/85 SMITH,FREDERICK P CA-SOLID; COMPASSIONATE				
L	Aug-16-85		AMENDMENT	85-29	DJF		850803
		(a)	CV,CKLST PT9 /003-076-022 UPDATED CV; PROT SUBM 1/18/85 BERTINO,JOSEPH CA-SOLID; COMPASSIONATE				

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16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Aug-21-85		AMENDMENT	85-30	DJF		850811
		(a)	CV(& ASSOCs),CKLST PT9a /003-076-023 PROT SUBM 1/18/85 VERDIRAME,JOSEPH CA-SOLID; COMPASSIONATE				
		(b)	CV-ASSOC(s) PT9b /003-079-001 4 ASSTs TO SRIDHAR (#178); CV & PROT SUBM 5/10/85				
		(c)	CV-ASSOC(s) PT9b /003-080-002 4 ASSTs TO BENEDETTO (#191 CV SUBM 7/8/85);PROT SUBM 5/10/85				
L	Sep-03-85		AMENDMENT	85-31	DJF		850865
		(a)	CKLST PT9a /003-076-020 PROT SUBM 1/18/85; CV(& ASSOCs) SUBM 5/29/85 PAPISH,STEPHEN W CA-SOLID; COMPASSIONATE				
		(b)	CV,CKLST PT9b /003-076-025 PROT SUBM 1/18/85 KUBOTA,THOMAS T CA-SOLID; COMPASSIONATE				
L	Sep-05-85		AMENDMENT	85-32	DJF		850866
		(a)	CV,CKLST PT9 /003-077-007 UPDATED CV; PROT SUBM 1/18/85 STUART,JOHN LEUKEMIA; COMPASSIONATE				
L	Sep-06-85		AMENDMENT	85-33	DJF		850760
		(a)	DRUG EXPERIENCE RPT PT10 /003-070-001 (FOLL UP TO 4/15/85 RPT) PT#25: TISSUE NECROSIS				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(b) DRUG EXPERIENCE RPT # /PT 10 (AUSTRALIA - COMPASSIONATE PT) TISSUE NECROSIS				
L	Sep-23-85		AMENDMENT	85-34	DJF		850840
			(a) CV(& ASSOCs),CKLST PT9a /003-077-010 PROT SUBM 1/10/85				
			(b) DRUG EXPERIENCE RPT # /PT 10 (WG) DEATH: OVERDOSE EFFECT; APLASIA BONE MARROW KOWAL-VERN,ARETA LEUKEMIA; COMPASSIONATE				
L	Sep-25-85		AMENDMENT	85-35	DJF		850965
			(a) CV,CKLST PT9 /003-076-018 PROT SUBM 1/18/85 SCHELL,FRANK CJ CA-SOLID; COMPASSIONATE				
			(b) PROTOCOL PT10a /003-075-000 FINAL COPY OF PROTOCOL, ORIGINALLY SUBM 2/22/84				
			(c) PROTOCOL AMENDMENT PT10b /003-075-000 A#2: DOSAGE ADJUSTMT; PROT (RE)SUBM 9/25/85, A#1 - 2/19/85				
L	Oct-11-85		AMENDMENT	85-36	DJF		850967
			(a) CV,CKLST PT9 /003-077-009 PROT SUBM 1/18/85 DENHAM,CLAUDE A LEUKEMIA; COMPASSIONATE				
L	Oct-16-85		AMENDMENT	85-37	DJF		850974
			(a) CV,CKLST PT9a /003-077-011 UPDATED CV; PROT SUBM 1/18/85 ARLIN, ZALMEN A LEUKEMIA; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(b) CV-ASSOC(s) PT9b /003-077-007 FOR 9 ASST INVESTIGATORS; PROT SUBM 1/18/85				
L	Oct-23-85		AMENDMENT	85-39	DJF		851018
			(a) SUMMARY, PRECLINICAL # /PT 6 ACUTE INTRAVESICULAR & INTRAPERITONEAL STUDIES IN DOGS (b) CV,CKLST,PROTO PT9 /003-082-001 DP3-78 REV'd/RESUBM'd 1/13/86 AS DP3-82; ALBERTS' CV 2/22/84 ALBERTS,DAVID S CA-BLADDER; DOSE RANGING INTRAVESIC ADMIN; DP3-78 REV'd & RESUBM'd 1/10/86 AS DP3-82				
L	Oct-23-85		AMENDMENT	85-38	DJF		851007
			(a) CV-ASSOC(s) PT9 /003-037-001 FOR LOCKER, TREATING PT #35 WHO MOVED FROM UCLA TO ILLINOIS				
L	Oct-25-85		AMENDMENT	85-40	DJF		851035
			(a) INVESTIGATOR BROCHURE # /PT 7 ISSUE DATE 10/15/85				
L	Oct-30-85		AMENDMENT	85-41	DJF		850969
			(a) CV,CKLST PT9a /003-076-033 PROT SUBM 1/18/85 DEUR,CHARLES J CA-SOLID; COMPASSIONATE				
			(b) CV,CKLST PT9b /003-076-026 UPDATED CV; PROT SUBM 1/18/85 MUGGIA,FANCO CA-SOLID; COMPASSIONATE				
			(c) CV,CKLST PT9c /003-076-024 PROT SUBM 1/18/85				

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16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

WALLACE,JAMES H
CA-SOLID; COMPASSIONATE

(d) CV,CKLST
PT9d /003-077-012
PROT SUBM 1/18/85
DeGREEN,PETER
LEUKEMIA; COMPASSIONATE

(e) CV(& ASSOCs),CKLST
PT9e /003-077-013
PROT SUBM 1/18/85
SCHECTER,GERALDINE
LEUKEMIA; COMPASSIONATE

(f) DRUG EXPERIENCE RPT
PT10 /003-044-002
PT # 5035 DEATH: JAUNDICE

L Nov-04-85 AMENDMENT 85-42 DJF 851093

(a) CV(& ASSOCs),CKLST
PT9 /003-046-006
WHEELER REPLACES GAMS AS PRINC INVEST; PROT SUBM 12/8/82
GAMS,RICHARD A
LYMPHOMA
NON-HODGKIN'S
WHEELER,RICHARD
LYMPHOMA
NON-HODGKIN'S

(b) CV(& ASSOCs),CKLST
PT9 /003-044-008
WHEELER REPLACES GAMS AS PRINC INVEST; PROT SUBM 9/10/82
GAMS,RICHARD A
LEUKEMIA

WHEELER,RICHARD
LEUKEMIA

L Nov-11-85 AMENDMENT 85-43 DJF 851101

(a) CV(& ASSOCs),CKLST
PT9 /003-076-032
COMPASSIONATE PROT SUBM 1/18/85

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16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

FIELDER,KATHLEEN
CA-SOLID; COMPASSIONATE

L Nov-14-85 AMENDMENT 85-44 DJF 851094

(a) CV,CKLST
PT9a /003-076-037
COMPASSIONATE PROT SUBM 1/18/85
ROSS,MICHAEL
CA-SOLID; COMPASSIONATE

(b) CKLST
PT9b /003-048-013
WHEELER (CV SUBM 11/4/85) REPLACES GAMS; PROT SUBM 2/14/83
GAMS,RICHARD A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WHEELER,RICHARD
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(c) CKLST
PT9b /003-071-028
WHEELER (CV SUBM 11/4/85) REPLACES GAMS; PROT SUBM 2/21/84
GAMS,RICHARD A
LYMPHOMA; vs m-BACOD m-BNCOD COMBO
WHEELER,RICHARD
LYMPHOMA; vs m-BACOD m-BNCOD COMBO

(d) CKLST
PT9b /003-074-011
WHEELER (CV & ASSOCs' SUBM 11/4/85) REPL GAMS; PROT 2/21/84
GAMS,RICHARD A
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)
WHEELER,RICHARD
ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Nov-18-85		AMENDMENT	85-45	DJF		851104
		(a)	CV(& ASSOCs),CKLST PT9a /003-076-034 COMPASSIONATE PROT SUBM 1/18/85 DANNEMAN,Wm G CA-SOLID; COMPASSIONATE				
		(b)	CV(& ASSOCs),CKLST PT9b /003-077-014 COMPASSIONATE PROT SUBM 1/18/85 STRAUSS,JAMES F LEUKEMIA; COMPASSIONATE				
F	Nov-18-85		REQUIREMENT FDA REQUIRES LED TO SUBMIT PAST PROGRESS REPORTS		DJF		851136
L	Nov-21-85		AMENDMENT	85-46	DJF		851116
		(a)	CKLST PT9 /003-076-035 CV SUBM 7/9/82; ASSOC CVs SUBM 7/9/82,10/27/83; PROT 1/18/85 LEVICK,STANLEY N CA-SOLID; COMPASSIONATE				
L	Nov-26-85	F Nov-18-85	CORRESPONDENCE LED IS INDEED UP TO DATE IN FILING PROGRESS REPORTS	85-47	DJF		851137
L	Dec-09-85		AMENDMENT	85-49	DJF		851176
		(a)	CV,CKLST PT9 /003-076-028 CV SUBM 3/11/85; PROT SUBM 1/11/85 McFARLAND,JAMES A CA-SOLID; COMPASSIONATE				
		(b)	CV,CKLST PT9 /003-076-046 CV SUBM 4/25/84; PROT SUBM 1/11/85				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			BENNETT,JOHN M CA-SOLID; COMPASSIONATE				
L	Dec-12-85		AMENDMENT	85-50	DJF		851192
		(a)	CV,CKLST PT9 /003-076-044 PROT SUBM 1/11/85 BALA,AYER CA-SOLID; COMPASSIONATE				
		(b)	CV(& ASSOCs),CKLST PT9 /003-076-045 PROT SUBM 1/11/85 PANDYA,KISHAN J CA-SOLID; COMPASSIONATE				
L	Dec-16-85		AMENDMENT	85-51	DJF		851214
		(a)	CV,CKLST PT9a /003-077-018 PROT SUBM 1/11/85 (UPDATED CV) SILVER,RICHARD T LEUKEMIA; COMPASSIONATE				
		(b)	CV,CKLST PT9b /003-076-051 PROT SUBM 1/11/85 HENDERSON,CHARLES A CA-SOLID; COMPASSIONATE				
L	Dec-23-85		AMENDMENT	85-53	DJF		851217
		(a)	CV(& ASSOCs),CKLST PT9 /003-074-025 PROT SUBM 2/21/84 RUBIN,ARNOLD D ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Jan-03-86		AMENDMENT	86-1	DJF		860011
		(a)	CV # /PT 9 CV FOR DR S SALETAN WHO REPLACES DUKART AS LED MONITOR				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
		(b)	PROTOCOL AMENDMENT PT10 /003-072-000 A#3: DELETION OF PK ANALYSES; PROT SUBM 12/13/83				
L	Jan-13-86		AMENDMENT	86-1	DJF		860547
		(a)	PROTOCOL PT10 /003-082-001 PROT REVISED (WAS 3-78) BASED ON TOXICITIES FROM CANADA STUD				
L	Jan-15-86		AMENDMENT	86-2	DJF		860548
		(a)	CV(& ASSOCs),CKLST PT9 /003-077-015 GRONCV,PAULA LEUKEMIA; COMPASSIONATE				
L	Jan-17-86		AMENDMENT	86-3	DJF		860549
		(a)	CV(& ASSOCs),CKLST PT9 /003-074-026 PROT SUBM 2/21/84 KATTLOVE,HERMAN ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Jan-29-86		AMENDMENT	86-4	DJF		860077
		(a)	CV,CKLST PT9a /003-076-021 PROT SUBM 1/11/85 PETERSON,JAY T CA-SOLID; COMPASSIONATE				
		(b)	CV,CKLST PT9b /003-077-019 PROT SUBM 1/11/85 HANSON,JOHN P LEUKEMIA; COMPASSIONATE				
L	Feb-03-86		AMENDMENT	86-5	DJF		860092
		(a)	CV,CKLST PT9a /003-076-049 PROT SUBM 1/11/85				

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16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			SCHREEDER,MARSHALL T CA-SOLID; COMPASSIONATE				
		(a)	CV,CKLST PT9b /003-076-043 PROT SUBM 1/11/85 SCHREEDER,MARSHALL T CA-SOLID; COMPASSIONATE				
L	Feb-05-86		AMENDMENT	86-6	DJF		860096
		(a)	CKLST PT9 /003-072-006 PROT SUBM 12/3/83; CV(& ASSOCs) SUBM 11/4/85 WHEELER,RICHARD H CA-BREAST; SPECIAL-PK INFLUENCE OF HEPATIC FUNCTION				
L	Feb-05-86		AMENDMENT	86-7	DJF		860095
		(a)	CV,CKLST PT9a /003-076-050 PROT SUBM 1/11/85 ALAVI,JANE B CA-SOLID; COMPASSIONATE				
		(b)	CV,CKLST PT9b /003-076-052 PROT SUBM 1/11/85 BLOW,ALTON J CA-SOLID; COMPASSIONATE				
L	Feb-18-86		AMENDMENT	86-8	DJF		860116
		(a)	CV(& ASSOCs),CKLST PT9 /003-074-027 PROT SUBM 2/21/84 BICKERS,JOHN N ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Feb-19-86		AMENDMENT	86-9	DJF		860102
		(a)	CV,CKLST PT9a /003-076-054 PROT SUBM 1/11/85				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			FEINER,ALAN S CA-SOLID; COMPASSIONATE				
			(b) CV,CKLST PT9a /003-076-062 PROT SUBM 1/11/85 FREDRIC,RHETT K CA-SOLID; COMPASSIONATE				
L	Feb-25-86		AMENDMENT	86-11	DJF		860148
			(a) CV(& ASSOCs),CKLST PT9 /003-076-048 PROT SUBM 1/1/86 HARRIS, WILLIAM KING,GERALD W CA-SOLID; COMPASSIONATE				
L	Feb-25-86		CORRESPONDENCE FDA AUTH'd TO X-REF IND FOR COOPER,STUART&PACIUCCI's FILING	86-10	DJF		860159
L	Mar-19-86		AMENDMENT LED PROPOSAL FOR EXPEDITING USE OF MITO ON COMPASSION BASIS	86-12	DJF		860215
L	Mar-19-86		AMENDMENT	86-13	DJF		860216
			(a) CKLST PT9a /003-076-036 GRACE'S CV SUBM 7/13/82; PROT SUBM 1/11/85 GRACE,WILLIAM R CA-SOLID; COMPASSIONATE				
			(b) CV,CKLST PT9b /003-076-040 PROT SUBM 1/11/85 ENGELBERG,CHARLES B CA-SOLID; COMPASSIONATE				
			(c) CV(& ASSOCs),CKLST PT9c /003-077-016 PROT SUBM 1/11/85				

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16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			O'CONNELL,JOSEPH LEUKEMIA; COMPASSIONATE				
L	Mar-20-86		AMENDMENT	86-15	DJF		860218
			(a) CV,CKLST PT9a /003-077-024 PROT SUBM 1/11/85 SENECAL,FRANCIS M LEUKEMIA; COMPASSIONATE				
			(b) CKLST,CV-ASSOC(s) PT9b /003-077-026 DESAI'S CV SUBM 11/18/85; PROT SUBM 1/11/85 DESAI,AJIT M LEUKEMIA; COMPASSIONATE				
			(c) CV,CKLST PT9c /003-077-032 PROT SUBM 1/11/85 MEARS,J GREGORY LEUKEMIA; COMPASSIONATE				
L	Mar-20-86		AMENDMENT	86-14	DJF		860217
			(a) CV(& ASSOCs),CKLST PT9a /003-076-047 PROT SUBM 1/11/85 GOODWIN,J WENDALL CA-SOLID; COMPASSIONATE				
			(b) CV,CKLST PT9b /003-076-053 PROT SUBM 1/11/85 STALLINGS,LAWRENCE M CA-SOLID; COMPASSIONATE				
			(c) CV,CKLST PT9c /003-076-061 PROT SUBM 1/11/85 McMAHON,RICHARD T CA-SOLID; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Mar-21-86		AMENDMENT	86-16	DJF		860219
		(a)	CV,CKLST PT9 /003-076-072 PROT SUBM 1/11/85 McKEOWN,JOHN M CA-SOLID; COMPASSIONATE				
L	Mar-31-86		AMENDMENT	86-17	DJF		860263
		(a)	CV(& ASSOCs),CKLST PT9 /003-072-007 PROT SUBM 12/13/83 BENNETT,JOHN M CA-BREAST; SPECIAL-PK INFLUENCE OF HEPATIC FUNCTION				
		(b)	PROTOCOL AMENDMENT PT10 /003-075-001 A#3: ALLOWS FOR CONTINUOUS (UNDRAINED) DWELL TIME				
L	Apr-09-86		AMENDMENT	86-18	DJF		860550
		(a)	CV(& ASSOCs),CKLST,PROT PT9,10 /003-081-001 HOLLAND,JAMES F CA-BREAST PHS I&II. COMBINATION OF NOVANTRONE w THIOTEPA &METHOTREXATE				
L	Apr-10-86		AMENDMENT	86-19	DJF		860339
		(a)	CV(& ASSOCs),CKLST PT9a /003-076-030 PROT SUBM 1/11/85 BEARDEN,JAMES D III CA-SOLID; COMPASSIONATE				
		(b)	CV(& ASSOCs),CKLST PT9b /003-076-065 PROT SUBM 1/11/85 NOMANBHOY,YUNUS T CA-SOLID; COMPASSIONATE				

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16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	Apr-15-86		AMENDMENT	86-20	DJF		860341
		(a)	CV,CKLST PT9 /003-076-060 PROT SUBM 1/11/85 HAROLD,SUSAN E CA-SOLID; COMPASSIONATE				
L	May-20-86		AMENDMENT	86-21	DJF		860493
		(a)	CV(& ASSOCs),CKLST PT9 /003-074-028 PROT SUBM 2/21/84 STEIN,RICHARD S ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	May-27-86		AMENDMENT	86-22	DJF		860512
		(a)	CV,CKLST PT9 /003-074-029 PROT SUBM 2/21/84 DARA,PARVEZ ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Jun-06-86		AMENDMENT	86-23	DJF		860551
		(a)	CV PT9a /003-082-001 UPDATED CV FOR ALBERTS & STANISIC (WHO IS NOW ASSOC INVESTR)				
		(b)	CV(& ASSOCs),CKLST PT9b /003-082-002 PROT SUBM 1/13/86 SHARIFI,R /LAMB,D CA-BLADDER; DOSE RANGING INTRAVESIC ADMIN; DP3-78 REV'd & RESUBM'd 1/10/86 AS DP3-82				
L	Jun-25-86		AMENDMENT	86-23	DJF		860612
		(a)	CKLST # /PT 9 LIST OF CURRENTLY ACTIVE INVESTIGATORS				

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(b) PROGRESS RPT # /PT 10a
ALSO, REFER TO SAFETY UPDATE SUBM'd 2/25/86 TO NDA 19-297
AHR,DAVID
CA-SOLID; COMPASSIONATE

ALAVI,JANE B
CA-SOLID; COMPASSIONATE

ALBALA,MAURICE
LEUKEMIA; COMPASSIONATE

ALI,I
LEUKEMIA; COMPASSIONATE

ALLEGRA/WOODCOCK
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
AMARE
LEUKEMIA

ARENA,PAUL
CA-SOLID; COMPASSIONATE

ARLIN, ZALMEN A
LEUKEMIA; COMPASSIONATE

ARLIN,ZALMEN A
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
ARMENTROUT,STEVEN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
ASBURY,ROBERT
CA-SOLID; COMPASSIONATE

BABCOCK,Wm
LEUKEMIA; COMPASSIONATE

BALA,AYER
CA-SOLID; COMPASSIONATE

BEARDEN,JAMES D III
CA-SOLID; COMPASSIONATE

BENEDETTO,PASQUALE
CA-STOMACH

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16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

BENIGNO,BENEDICT R
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BENJAMIN,ROBERT
CA-SOLID; COMPASSIONATE

BENNETT,JOHN M
CA-SOLID; COMPASSIONATE

BERNARD,STEPHEN A
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
BERNARD,STEPHEN A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BERTINO,JOSEPH
CA-SOLID; COMPASSIONATE

BIRDWELL,ROBERT
CA-SOLID; COMPASSIONATE

BITRAN,JACOB /GOLOMB
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
BLOCK
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
BLOW,ALTON J
CA-SOLID; COMPASSIONATE

BLUMING,AVRUM Z
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
BRADY,ALBERT
CA-SOLID; COMPASSIONATE

BRODORSKY
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
BUDD,THOMAS G
CA-SOLID; COMPASSIONATE

BURTON,GARY
LEUKEMIA; COMPASSIONATE

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16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

CASIMIR,MIRTHA
CA-SOLID; COMPASSIONATE

CHLEBOWSKI
HEPATOMA

CHU,ALBERT
LEUKEMIA; COMPASSIONATE

COLEMAN,MORTON
CA-SOLID; COMPASSIONATE

CONRAD,MARCEL E
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
CONRAD,MARCEL E
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
COOPER,MILES R
LEUKEMIA; COMPASSIONATE

COSTANZI,JOHN J
LYMPHOMA
NON-HODGKIN'S
CUSTER,GALEN
LEUKEMIA; COMPASSIONATE

CUTTNER,JANET
LEUKEMIA; COMPASSIONATE

DANNEMAN,Wm G
CA-SOLID; COMPASSIONATE

DAO
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
DARA,PARVEZ
CA-SOLID; COMPASSIONATE

DAVIS,HUGH
CA-SOLID; COMPASSIONATE

DEAN,HERBERT
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

DENEFRIO,JOHN M
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
DENEFRIO,JOHN M
CA-SOLID; COMPASSIONATE

DENES,ALEX E
CA-SOLID; COMPASSIONATE

DENHAM,CLAUDE A
LEUKEMIA; COMPASSIONATE

DESAI,AJIT M
LEUKEMIA; COMPASSIONATE

DEUR,CHARLES
LEUKEMIA; COMPASSIONATE

DEUR,CHARLES J
CA-SOLID; COMPASSIONATE

DICKMAN,ELLIOT
CA-SOLID; COMPASSIONATE

DOROSHOW
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
DOTY,GORDON L
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
DOTY,GORDON L
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
DUGAN
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
DeGREEN,PETER
LEUKEMIA; COMPASSIONATE

ENGELBERG,CHARLES B
CA-SOLID; COMPASSIONATE

ERSLEV,ALLAN J
LEUKEMIA

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

FEINER,ALAN S
CA-SOLID; COMPASSIONATE

FIELDER,KATHLEEN
CA-SOLID; COMPASSIONATE

FLETCHER,Wm
CA-SOLID; COMPASSIONATE

FOOTE,SANDRA
CA-SOLID; COMPASSIONATE

FORTE,FRANCIS A
CA-SOLID; COMPASSIONATE

FORTE,FRANCIS A
LEUKEMIA; COMPASSIONATE

FREDRIC,RHETT K
CA-SOLID; COMPASSIONATE

FRIEDMAN,ALLAN
LEUKEMIA; COMPASSIONATE

GEILS,GEORGE
LEUKEMIA; COMPASSIONATE

GEORGE,SEBASTIAN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GOCKERMAN,JOHN
LEUKEMIA; COMPASSIONATE

GOODMAN,GARY E
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
GOODWIN,J WENDALL
CA-SOLID; COMPASSIONATE

GOTTLEIB,ROBERT J
CA-SOLID; COMPASSIONATE

GRACE,WILLIAM R
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
GRACE,WILLIAM R
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Event Due	ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

GRACE,WILLIAM R
CA-SOLID; COMPASSIONATE

GRANATIR,ROBERT
LEUKEMIA; COMPASSIONATE

GRONCY,PAULA
LEUKEMIA; COMPASSIONATE

HAN,DIN
LEUKEMIA; COMPASSIONATE

HANSON,JOHN P
LEUKEMIA; COMPASSIONATE

HANSON,JOHN P
CA-SOLID; COMPASSIONATE

HANSON,KARL
CA-SOLID; COMPASSIONATE

HAROLD,SUSAN E
CA-SOLID; COMPASSIONATE

HENDERSON,CHARLES A
CA-SOLID; COMPASSIONATE

HENDERSON,I CRAIG
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
HESKETH,PAUL
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
HOLLAND,JAMES F
ALL
COMBINED w/ VINCRISTINE & DEXAMETHASONE
HOLROYDE,CRISTPHER P
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
HORVATH,WILLIAM L
CA-SOLID; COMPASSIONATE

HURD,DAVID
CA-SOLID; COMPASSIONATE

HYMAN,PAUL
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

JAFFREY,IRA S
CA-SOLID; COMPASSIONATE

JAFFREY,IRA S
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
JIM,ROBERT T.S.
LEUKEMIA; COMPASSIONATE

JONES,ROY
CA-BREAST; DOSE RANGING
ESCALATING DOSE -CARDIAC MEASUREMENTS
KAJANI,M
LEUKEMIA; COMPASSIONATE

KAPLAN,BARRY
CA-SOLID; COMPASSIONATE

KELSEN,DAVID
CA-STOMACH

KENNEALEY,GERARD
CA-SOLID; COMPASSIONATE

KING,GERALD W
CA-SOLID; COMPASSIONATE

KOO,VICTOR S
CA-SOLID; COMPASSIONATE

KOWAL-VERN,ARETA
LEUKEMIA; COMPASSIONATE

KRAKOFF,I H
CA-BREAST
COMB w/ CYCLOPHOS, 5-FU X-OVER TO
ADRIAMYCIN/VINBLASTINE
KRAKOFF,I H
KREMENTZ,EDWARD T
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
KUBOTA,THOMAS T
CA-SOLID; COMPASSIONATE

LAWSON
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

LEE,EDWARD
LEUKEMIA; COMPASSIONATE

LEVICK
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
LEVICK,STANLEY N
CA-SOLID; COMPASSIONATE

LEVINE,JAMES D
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
LOCKER,GERSHON
CA-SOLID; COMPASSIONATE

LOWENBRAUN,STANLEY
CA-SOLID; COMPASSIONATE

MABRY,R JAMES
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
MEARS,J GREGORY
LEUKEMIA; COMPASSIONATE

MENA,PAUL
CA-SOLID; COMPASSIONATE

MINTON,JOHN
CA-SOLID; COMPASSIONATE

MOORE,ANN
CA-SOLID; COMPASSIONATE

MOORE,JOSEPH
LEUKEMIA; COMPASSIONATE

MOORE,JOSEPH O
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
MORGAN,LEE ROY
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
MUGGIA,FRANCO
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

MUSS
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
MYERS,ALAN
CA-SOLID; COMPASSIONATE

McFARLAND,JAMES A
LEUKEMIA; COMPASSIONATE

McFARLAND,JAMES A
CA-SOLID; COMPASSIONATE

McKEOWN,JOHN M
CA-SOLID; COMPASSIONATE

McMAHON,RICHARD T
CA-SOLID; COMPASSIONATE

NELSON,ERIC C
CA-SOLID; COMPASSIONATE

NOMANBHOY,YUNUS T
CA-SOLID; COMPASSIONATE

O'CONNELL,JOSEPH
LEUKEMIA; COMPASSIONATE

PANDYA,KISHAN J
CA-SOLID; COMPASSIONATE

PAPISH,STEPHEN W
LEUKEMIA; COMPASSIONATE

PAPISH,STEPHEN W
CA-SOLID; COMPASSIONATE

PARISER,SANFORD
LEUKEMIA; COMPASSIONATE

PAULSON,STEVEN
LEUKEMIA; COMPASSIONATE

PETERSON,JAY T
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

PLOTKIN,DAVID
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PORTLOCK,CAROL S
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
PRESANT,CARY A
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-N-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
RIDDICK,DAVID
CA-SOLID; COMPASSIONATE

RIES,CURT
LEUKEMIA; COMPASSIONATE

ROACH,RALPH W
ROBERTS,JOHN
CA-SOLID; COMPASSIONATE

ROEDER,MICHAEL
CA-SOLID; COMPASSIONATE

ROSS
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
ROSS,MICHAEL
CA-SOLID; COMPASSIONATE

ROZEN,SIMON
LEUKEMIA; COMPASSIONATE

RYMER,Wm
CA-SOLID; COMPASSIONATE

SARTIANO,GEORGE P
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
SAUNDERS,DARRELL F
LEUKEMIA; COMPASSIONATE

SCHECTER,GERALDINE
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event	Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND			MITOXANTRONE CL 232,315 ANTICANCER AGENT				

SCHELL,FRANK CJ
CA-SOLID; COMPASSIONATE

SCHER,NANCY
CA-SOLID; COMPASSIONATE

SCHREEDER,MARSHALL T
CA-SOLID; COMPASSIONATE

SCHWARTZ,JOEL
CA-SOLID; COMPASSIONATE

SEEGER,JARELL
CA-SOLID; COMPASSIONATE

SENECAL,FRANCIS M
LEUKEMIA; COMPASSIONATE

SHAW,JOHN
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
SHERMAN,ALFRED I
CA-SOLID; COMPASSIONATE

SHIFTAN,THOMAS
CA-SOLID; COMPASSIONATE

SILVER
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
SILVER,RICHARD T
LEUKEMIA; COMPASSIONATE

SMITH,FREDERICK P
CA-SOLID; COMPASSIONATE

STALLINGS,LAWRENCE M
CA-SOLID; COMPASSIONATE

STASZEWSKI,HARRY
LEUKEMIA; COMPASSIONATE

STEIN,RICHARD S
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO
STONE,LAWRENCE A
LYMPHOMA; vs m-BACOD
m-BNCOD COMBO

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			STRAUSS,JAMES F LEUKEMIA; COMPASSIONATE				
			STUART,JOHN LEUKEMIA; COMPASSIONATE				
			TALARICO,LILIA LEUKEMIA; COMPASSIONATE				
			THOMAS,PAUL LEUKEMIA; COMPASSIONATE				
			VERDIRAME,JOSEPH CA-SOLID; COMPASSIONATE				
			VINCEGUERRA,VINCENT LEUKEMIA; COMPASSIONATE				
			VOGEL,CHARLES CA-SOLID; COMPASSIONATE				
			VOGEL,CHARLES L CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU VOLBERDING CA-BREAST; vs ADRIAMYCIN MULTI-CTR 2nd LINE PTS VOYCE,GARY F LYMPHOMA; vs m-BACOD m-BNCOD COMBO WACHI,DENNIS H LYMPHOMA; vs m-BACOD m-BNCOD COMBO WALLACE,JAMES H CA-SOLID; COMPASSIONATE				
			WEAVER,ZEBULON III CA-SOLID; COMPASSIONATE				
			WEIDEN CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-N-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU WEINBERG,BRUCE LEUKEMIA; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				

WHEELER,R (/GAMS)
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WHEELER,RICHARD
LEUKEMIA

WHITE
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
WHITE,CHARLES F
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WHITE,CHARLES F
LYMPHOMA; vs m-BACOD
m-BMCOD COMBO
WIERNIK,PETER H
LYMPHOMA; vs m-BACOD
m-BMCOD COMBO
WILBUR,DAVID
CA-SOLID; COMPASSIONATE

WILLIAMS,THOMAS
CA-SOLID; COMPASSIONATE

WOLF,DAVID
LEUKEMIA; COMPASSIONATE

WOLFF,STEVEN N
CA-BREAST; vs ADRIAMYCIN
MULTI-CTR 2nd LINE PTS
WOLFF,STEVEN N
LYMPHOMA; vs m-BACOD
m-BMCOD COMBO
WOLFF,STEVEN N
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU
WOODCOCK,THOMAS M
LYMPHOMA; vs m-BACOD
m-BMCOD COMBO
WORTMAN,JAMES
CA-SOLID; COMPASSIONATE

ZALUSKY,RALPH
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(c) CLINICAL STUDIES PT10b /003-076-000 STATUS OF STUDY DOCUMENTN OF COMPASSION SOLID TUMORS STUDIES				
			(d) CLINICAL STUDIES PT10b /003-077-000 STATUS OF STUDY DOCUMENT'N OF COMPASSIONATE LEUKEMIA STUDIES				
L	Jul-03-86	T Jul-01-86	CORRESPONDENCE SUMMARY/LISTING OF LOTS USED IN PRESERV-EFF EVALUATION TESTS		GRP		860764
L	Jul-15-86		AMENDMENT	86-25	DJF		860668
			(a) INVESTGTR DOCUMENTN AT LEDERLE PT9 /003-076-000 PROT SUBM 1/11/85				
			(b) INVESTGTR DOCUMENTN AT LEDERLE PT9 /003-077-000 PROT SUBM 1/11/85				
L	Aug-05-86		AMENDMENT FDA AUTHd TO X-REF OUR IND TO SUPPORT CAPIZZI's IND FILING	86-26	DJF		870744
L	Aug-06-86		AMENDMENT	86-25	DJF		870743
			(a) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-000 LIST OF INVESTGTRs RECEIVING DRUG DURING JULY,'86 BROWN,B.S. CA-SOLID; COMPASSIONATE CARDAMONE,JOSEPH CA-SOLID; COMPASSIONATE HOLLISTER,DICKERMAN LEUKEMIA; COMPASSIONATE LEIBOWITC,R CA-SOLID; COMPASSIONATE LINK,JOHN CA-SOLID; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

MUCHMORE,ELAINE
CA-SOLID; COMPASSIONATE

McDONALD,C
CA-SOLID; COMPASSIONATE

(b) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-000
LIST OF INVSTGTRs RECEIVING DRUG DURING JULY,'86
EYSTER,ELAINE
LEUKEMIA; COMPASSIONATE

KOPEL,SAM
LEUKEMIA; COMPASSIONATE

POLMEROY,T.
LEUKEMIA; COMPASSIONATE

RUBIN,ARNOLD
LEUKEMIA; COMPASSIONATE

SCHARFMAN,WILLIAM
LEUKEMIA; COMPASSIONATE

VONHOFF,DANIEL
LEUKEMIA; COMPASSIONATE

F Aug-11-86	L Jul-03-86	REQUIREMENT		GRP		860720

(a) PRESERVATIVE EFFICACY
LED MUST CLARIFY COMPOSITN/MTD OF MANUF FOR
FORMULNS 24E,23R

L Aug-14-86		AMENDMENT	86-27	DJF		870742

(a) CKLST
PT9 /003-048-001
CKLST FOR DR. GREEN WHO IS REPLACING MUGGIA AS
PRINC INVSTGR
GREEN,M
CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO)
CYCLOPHOSPHAMIDE-M-5FU vs
CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU

(b) INVESTIGATOR REPLACEMENT
PT9 /003-048-001
MUGGIA REPLACED BY GREEN

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			MUGGIA,FRANCO CA-BREAST; vs ADRIAMYCIN (AS PART OF A COMBO) CYCLOPHOSPHAMIDE-M-5FU vs CYCLOPHOSPHAMIDE-ADRIAMYCIN-5FU				
L	Aug-18-86	F Aug-11-86	CORRESPONDENCE		GRP		860721
			(a) PRESERVATIVE EFFICACY CLARIFICATION OF COMPOSITION/MANUf'g re PRESERV EFF EVALUATN				
L	Sep-02-86		AMENDMENT	86-28	DJF		870702
			(a) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-000 LIST OF INVESTIGATORS RECEIVING DRUG DURING AUGUST,'86 BERNARD,STEPHEN CA-SOLID; COMPASSIONATE BRADY,ALBERT CA-SOLID; COMPASSIONATE CHERNOF,DAVID CA-SOLID; COMPASSIONATE CHLEBOWSKI,JOAN CA-SOLID; COMPASSIONATE FLIPPIN,ANTHONY LEUKEMIA; COMPASSIONATE GRUNDBERG,STEVEN CA-SOLID; COMPASSIONATE MANUSZAK,PAUL CA-SOLID; COMPASSIONATE MILLER,DONALD CA-SOLID; COMPASSIONATE OZA,YAGNESH CA-SOLID; COMPASSIONATE RENTSCHLER,ROBERT CA-SOLID; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

SCHNUR,GARY
CA-SOLID; COMPASSIONATE

WORKMAN,FRANK
CA-SOLID; COMPASSIONATE

(b) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-000
LIST OF INVESTIGATORS REC'd EMERGENCY DRUG SHIPMT IN AUG.'86
ALLAN,STEVE
LEUKEMIA; COMPASSIONATE

BITRAN,JACOB
LEUKEMIA; COMPASSIONATE

BRASS,LAWRENCE
LEUKEMIA; COMPASSIONATE

KATZ,MARTIN
LEUKEMIA; COMPASSIONATE

KELLERMEYER,ROBERT
LEUKEMIA; COMPASSIONATE

(c) INVESTGTR DOCUMENTN at LEDERLE
PT9 /003-077-000
INVESTIGATOR DOCUMENTN NOW ON FILE (PREVIOUSLY SHIPPED DRUG)
BURTON,GARY
LEUKEMIA; COMPASSIONATE

MOORE,JOSEPH
LEUKEMIA; COMPASSIONATE

WEINBERG,J
LEUKEMIA; COMPASSIONATE

L Sep-09-86 AMENDMENT 86-29 DJF 860828

(a) CV(& ASSOCs),CKLST,PROT
PT9a,10 /003-084-001
CAPIZZI,ROBERT
LEUKEMIA; vs ARA-C, ASPARAGINASE
MITO IN AMLL, ALL, CBL-BL

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			(b) CV(& ASSOCs),CKLST,PROT PT9a,10 /003-084-002				
L	Oct-01-86		AMENDMENT	86-31	DJF		861028
			(a) CV(& ASSOCs),CKLST PT9 /003-084-003 PROT SUBM 9/9/86 RAAB,STEPHEN LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-BL				
L	Oct-02-86		AMENDMENT	86-30	DJF		860931
			(a) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-115 RECEIVED NOVANTRONE DURING SEPTEMBER, 1986 WOZNIK,ANTIONETTE CA-SOLID; COMPASSIONATE				
			(b) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-116 RECEIVED NOVANTRONE DURING SEPTEMBER, 1986 PUGH,REGINALD CA-SOLID; COMPASSIONATE				
			(c) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-117 RECEIVED NOVANTRONE DURING SEPTEMBER, 1986 LEWIN,MARGARET CA-SOLID; COMPASSIONATE				
			(e) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-118 RECEIVED NOVANTRONE DURING SEPTEMBER, 1986 KRONER,JOAN CA-SOLID; COMPASSIONATE				
			(f) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-119 RECEIVED NOVANTRONE DURING SEPTEMBER, 1986 BOHNEN,ROBERT CA-SOLID; COMPASSIONATE				
			(g) INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-120 RECEIVED NOVANTRONE DURING SEPTEMBER, 1986				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

NICHOLS,CRAIG
CA-SOLID; COMPASSIONATE

(h) INVESTGTR DOCUMENTN at LEDERLE
PT9 /003-076-121
RECEIVED NOVANTRONE DURING SEPTEMBER, 1986
PARKER,BARBARA
CA-SOLID; COMPASSIONATE

(i) INVESTGTR DOCUMENTN at LEDERLE
PT9 /003-076-122
RECEIVED NOVANTRONE DURING SEPTEMBER, 1986
BRONER,MARTIN
CA-SOLID; COMPASSIONATE

(j) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-070
REC'd EMERGENCY DRUG SHIPMENTS 9/86; PROPER DOCUMENTN COMING
BHARDWHA,SUSHIL
LEUKEMIA; COMPASSIONATE

(k) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-071
REC'd EMERGENCY DRUG SHIPMENTS 9/86; PROPER DOCUMENTN COMING
BEDROSE,ANTRANIK
LEUKEMIA; COMPASSIONATE

(l) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-072
REC'd EMERGENCY DRUG SHIPMENTS 9/86; PROPER DOCUMENTN COMING
CASSILETH,PETER
LEUKEMIA; COMPASSIONATE

(m) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-073
REC'd EMERGENCY DRUG SHIPMENTS 9/86; PROPER DOCUMENTN COMING
OLSON,JOHN
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

(a) CV
PT9a /003-082-002
CV FOR LAMB, NEW CO-INVESTIGTR TO SHARIFI; PROT SUBM 1/10/86
SHARIFI R/ LAMB D
CA-BLADDER; DOSE RANGING
INTRAVESIC ADMIN; DP3-78 REV'd & RESUBM'd 1/10/86 AS DP3-82

(b) CV
PT9b /003-072-002
CV FOR ALI, NEW CO-INVSTGTR TO CHLEBOWSKI; PROT SUBM 12/3/83
CHLEBOWSKI/ ALI I
CA-BREAST; SPECIAL-PK
INFLUENCE OF HEPATIC FUNCTION

(c) CV
PT9c /003-046-002
CV FOR MILLER, NEW CO-INVSGTR TO PETERSON; PROT SUBM 12/8/82
PETERSON / MILLER
LYMPHOMA
NON-HODGKIN'S

L Oct-21-86 CORRESPONDENCE 86-32 DJF 861034
FDA AUTH'd TO X-REF IND pts. 1-6 TO SUPPORT CHAMPIN'S FILING

L Oct-24-86 AMENDMENT 86-33 DJF 860969

(a) CV(& ASSOCs),CKLST
PT9 /003-084-004
PROT SUBM 9/9/86
TODD,MARY B
LEUKEMIA; vs ARA-C, ASPARAGINASE
MITO IN ANLL, ALL, CBL-BL

L Nov-04-86 AMENDMENT 86-35 DJF 870703

(a) INVESTGTR DOCUMENTN at LEDERLE/003-076-0
LIST OF INVESTIGATORS REC'g DRUG DURING OCTOBER '86
BROOKS,BARRY
CA-SOLID; COMPASSIONATE

BUTLER,FRED O
CA-SOLID; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

CARPENTER,JOHN
CA-SOLID; COMPASSIONATE

HARWIN,WILLIAM
CA-SOLID; COMPASSIONATE

KISIELIUS,THOMAS
CA-SOLID; COMPASSIONATE

LYSS,ALAN
CA-SOLID; COMPASSIONATE

NEEDLES,BURTON M
CA-SOLID; COMPASSIONATE

RAPHAEL,BRUCE
CA-SOLID; COMPASSIONATE

SPICER,DARCY
CA-SOLID; COMPASSIONATE

(b) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-000
INVESTIGATORS REC'q EMERGENCY DRUG SHIPMENT DURING OCT.'86
PEMBERTON,CLIFFORD
LEUKEMIA; COMPASSIONATE

PIETRAGALLO,LOUIS
LEUKEMIA; COMPASSIONATE

RAGAB,ABDEL
LEUKEMIA; COMPASSIONATE

SPALDING,MONICA
LEUKEMIA; COMPASSIONATE

(c) INVESTGTR DOCUMENTN at LEDERLE/003-077-0
INVESTIGATOR DOCUMENTN NOW ON FILE (PREVIOUSLY SHIPPED DRUG)
ALLAN,STEVE
LEUKEMIA; COMPASSIONATE

BRASS,LAWRENCE
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			SYSTER,ELAINE LEUKEMIA; COMPASSIONATE				
			FELBER,NORBERT LEUKEMIA; COMPASSIONATE				
			FLIPPIN,ANTHONY LEUKEMIA; COMPASSIONATE				
			HOLLISTER,DICKERMAN LEUKEMIA; COMPASSIONATE				
			SCHARFMAN,WILLIAM LEUKEMIA; COMPASSIONATE				
			VON HOFF,DANIEL LEUKEMIA; COMPASSIONATE				
L	Nov-13-86		AMENDMENT	86-37	DJF		870716
		(a)	CV(& ASSOCs),CKLST PT9 /003-082-003 DP 3-82 SUBM 1/13/86 SARDSDY,MICHAEL CA-BLADDER; DOSE RANGING INTRAVESIC ADMIN; DP3-78 REV'd & RESUBM'd 1/10/86 AS DP3-82				
L	Nov-25-86		AMENDMENT	86-38	DJF		870722
		(a)	PHARMACY BROCHURE # /PT 7 UPDATED PHARMACY BROCHURE				
		(b)	DER NARRATIVE PT10 /003-075-001 pts# 31-33,35: DEVELOPED INTESTINAL OBSTRUCT (DOSE-LIM TOX)				
L	Dec-05-86		AMENDMENT	86-39	DJF		870730
		(a)	INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-000 RECEIVED EMERGENCY DRUG SHIPMENT DURING NOVEMBER,'86 BERTOLI,JOSEPH CA-SOLID; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

CABANILLAS,FERNANDO
CA-SOLID; COMPASSIONATE

CAMPOS,LUIS
CA-SOLID; COMPASSIONATE

HILL,LAWRENCE
CA-SOLID; COMPASSIONATE

POPOVIC,WILLIAM
CA-SOLID; COMPASSIONATE

SPURR,CHARLES
CA-SOLID; COMPASSIONATE

(b) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-000
RECEIVED EMERGENCY DRUG SHIPMENT DURING NOV.'86
GADUZDA,THOMAS
LEUKEMIA; COMPASSIONATE

HINES,JOHN
LEUKEMIA; COMPASSIONATE

HINES,JOHN
LICHTMAN,STUART
LEUKEMIA; COMPASSIONATE

MAZZA,JOSEPH
LEUKEMIA; COMPASSIONATE

NACHANT,NEIL
LEUKEMIA; COMPASSIONATE

PONE,JACOB
LEUKEMIA; COMPASSIONATE

TISMAN,GLEN
LEUKEMIA; COMPASSIONATE

(c) INVESTGTR DOCUMENTN at LEDERLE
PT9 /003-077-000
DOCUMENTATION NOW ON FILE (PREVIOUSLY SHIPPED DRUG)
CAPIZZI,ROBERT
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp	Event Due	Event ID

16,332 IND MITOXANTRONE CL 232,315 ANTICANCER AGENT

KELLERMEYER,ROBERT
LEUKEMIA; COMPASSIONATE

(d) DER NARRATIVE
PT10 /003-075-001
11/25/86 DER SHOULD HAVE CITED OVARIAN CANCER AS INDICATION

L Jan-20-87 AMENDMENT 87-1 DJF 861315
MONTHLY UPDATE FOR DEC '86 OF COMPASSIONATE USE 3-76,3-77

(a) INVESTGTR DOCUMENTN at LEDERLE
PT9 /003-076-000
PROTOCOL 3-76 COMPASSIONATE USE / REC'D DEC 86
AJAIKUMAR, B.S.
CA-SOLID; COMPASSIONATE

FURST, ANNETTE
CA-SOLID; COMPASSIONATE

GEERAERTS, LOUIS
CA-SOLID; COMPASSIONATE

LUBDKE, DAN
CA-SOLID; COMPASSIONATE

LUNDBERG W.BRUCE
CA-SOLID; COMPASSIONATE

PATTON, ALLEN
CA-SOLID; COMPASSIONATE

STASZEWSKI, HARRY
CA-SOLID; COMPASSIONATE

TISMAN, GLENN
CA-SOLID; COMPASSIONATE

(b) INVESTGTR DOCUMENTN PENDING
PT9 /003-077-000
PROTOCOL 3-77 COMPASSIONATE USE
AHMED, FARDUK
LEUKEMIA; COMPASSIONATE

CARTER, PETER
LEUKEMIA; COMPASSIONATE

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				

CRAUT, ERIC
LEUKEMIA; COMPASSIONATE

HYMES, KENNETH
LEUKEMIA; COMPASSIONATE

JHANGANI, HARESH
LEUKEMIA; COMPASSIONATE

KLEIN, LEONARD
LEUKEMIA; COMPASSIONATE

KLEIN, LEONARD
LEUKEMIA; COMPASSIONATE

KNOSPE, WILLIAM
LEUKEMIA; COMPASSIONATE

RICHMOND, CAROL
LEUKEMIA; COMPASSIONATE

STOLBERG,LAWRENCE
LEUKEMIA; COMPASSIONATE

STOLBERG,LAWRENCE
LEUKEMIA; COMPASSIONATE

ZEHNGEHOT, LEE
LEUKEMIA; COMPASSIONATE

(c) INVESTGTR DOCUMENTN at LEDERLE
PT9 /003-077-000
PROTOCOL 3-77 COMPASSIONATE USE / REC'D DEC 86
BITRAN, JACOB
LEUKEMIA; COMPASSIONATE

KATZ, MARTIN
LEUKEMIA; COMPASSIONATE

RUBIN, ARNOLD
LEUKEMIA; COMPASSIONATE

L Feb-04-87		AMENDMENT	87-2	DJF		861301

(a) CV(& ASSOCs),CKLST
PT9 /003-084-005
PROT SUBMITTED 9/9/86

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			STUART, ROBT LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-BL				
L	Feb-25-87		AMENDMENT	87-3	DJF		870083
			MTHLY UPDATE FOR JAN '87/COMP. USE PROTS 3-76 / 3-77				
			(a) INVESTGTR DOCUMENTN at LEDERLE # /PT 9 PROT 3-76 COMP USE / REC'D JAN '87				
			(b) INVESTGTR DOCUMENTN PENDING # /PT 9 PROT 3-77 COMPASSIONATE USE				
			(c) INVESTGTR DOCUMENTN at LEDERLE # /PT 9 PROT 3-77 COMPASSIONATE USE / REC'D JAN '87				
L	Mar-06-87		AMENDMENT	87-4	DJF		870089
			(a) CV(& ASSOCs),CKLST,PROT PT9, 10 /003-087-001 PROTOCOL #3-87 CHEMO-HORMONAL IN ADV BREAST CA ALLEGRA, JOS. C. CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO EPREMIAN, BARBARA E CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO GENTILE, PATRICK S. CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO HAMM, JOHN T. CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO SEEGER, JANALL CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Even ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			SHETH, SUBHASH P. CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO WOODCOCK, THOS, M. CA-BREAST COMB c TAMOX PREMARIN MTX 5-FU LEUCOVORIN CA-BREAST REQUESTED BY DR G.BURKE,MRO				
L	Mar-16-87		CORRESPONDENCE FDA AUTH'D TO X-REF IND FOR PATT'S FILING.	87-5	DJF		870979
			(a) CV PI-YEHUDA PATT PATT, YEHUDA				
L	Mar-23-87		AMENDMENT PI- ARNOLD RUBIN	87-6	DJF		870973
			(a) CV(& ASSOCs) PI- ARNOLD RUBIN TREATNG-ACUTE NONLYMPHOCYTIC LEUKEMIA FERNBACH, BARRY ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE) RUBIN, ARNOLD ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE) YAMUSAH, EMANUEL ANLL; vs CERUBIDINE & CYTOSAR (ARA-C) IN COMBO W CYTOSAR (ARA-C)(CYTARABINE)				
L	Apr-01-87		CORRESPONDENCE	87-7	DJF		870945
			(a) PRECLINICAL # /PT 10 NOVANTRONE USED TO TREAT HEPATOCELLULAR CARCINOMA RATAIN, MARK J. (b) COMPONENTS & COMPOSITION # /PT 10 HEPATOCELLULAR CARCINOMA (c) CHEMISTRY # /PT 10 (d) MANUF & CONTROLS # /PT 10 (e) CLINICAL STUDIES # /PT 10				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND	MITOXANTRONE	CL 232,315 ANTICANCER AGENT				
L	May-14-87		AMENDMENT	87-8	DJF		870637
			(a) PROTOCOL AMENDMENT PT10 /003-087-001 RADIONUCLIDE SCAN DNE BE4 TREATMNT CYCL WHEN NOV.> 120MG/M2				
L	May-22-87		AMENDMENT	87-9	DJF		870635
			(a) DRUG EXPERIENCE RPT PT10 /003-076-149 OVERDOSE OF NOVANTRONE -FEMALE PAT.-COMP.PROT. BREAST CANCER				
			(b) PROTOCOL PT10 /003-084-000 STUDY WAS STOPPED DUE TO 2 PATIENTS DEATHS				
			(c) TRIAL-SITE(S) CLOSED /003-084-0 STUDY 3-84 (ALL SITES 1-5) DISCONTINUED DUE TO DEATHS CAPIZZI,ROBERT LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-BL HAMPTON,JAMES W LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-RL RAAB,STEPHEN LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-RL STUART, ROBERT LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-BL TODD,MARY B LEUKEMIA; vs ARA-C, ASPARAGINASE MITO IN ANLL, ALL, CBL-BL				
L	May-29-87		AMENDMENT PI- MAURIE MARKMAN-TREATNG OVARIAN CANCER	87-10	DJF		870634
			(a) CV # /PT 9 MARKMAN TREATNG PAT.W/OVARIAN CANCER USING INTRAPERITON.RTE. MARKMAN, MAURIE				
			(a) CV PI-MAURIE MARKMAN/TREATNG OVARIAN CANCER,INTRAPERITONEAL RT.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			MARKMAN, MAURIE				
L	Jun-03-87		AMENDMENT	87-11	DJF		870633
		(a)	PROTOCOL AMENDMENT PT10 /003-081-001 PHASE II-II STDY W/TNM IN PAT.W/ RECURRENT &METAST.BRST CANC				
L	Jun-08-87		AMENDMENT INV/COMP USE	87-12	DJF		870775
		(a)	INVESTGTR DOCUMENTN at LEDERLE PT9 /003-076-000 INV LIST RECD DRUG FROM FEB-MAY '87 (#s 155 THRU 177) BOYLE, RAMONN CA-SOLID; COMPASSIONATE ALLEN SL CA-SOLID; COMPASSIONATE BASWELL, JOHN CA-SOLID; COMPASSIONATE BROWNE, KENNEDY CA-SOLID; COMPASSIONATE CIMO, PHILIP CA-SOLID; COMPASSIONATE FANGMAN, MICHAEL CA-SOLID; COMPASSIONATE FISHER, JJ CA-SOLID; COMPASSIONATE FORSCHER, CHARLES CA-SOLID; COMPASSIONATE GUY, JERRY T CA-SOLID; COMPASSIONATE HALPERIN, JOSEPH CA-SOLID; COMPASSIONATE				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
			HAYWARD, M CA-SOLID; COMPASSIONATE				
			HURTUBISE, MICHEL CA-SOLID; COMPASSIONATE				
			JENKINS, JAY CA-SOLID; COMPASSIONATE				
			KAYE, STEPHEN CA-SOLID; COMPASSIONATE				
			MANDEL, EUGENE CA-SOLID; COMPASSIONATE				
			MARILLEY, RALPH CA-SOLID; COMPASSIONATE				
			MOYNIHAN, J CA-SOLID; COMPASSIONATE				
			PRASTHOFER, EDW CA-SOLID; COMPASSIONATE				
			RYAN, THOMAS CA-SOLID; COMPASSIONATE				
			SAWKAR, LAXMIDAS CA-SOLID; COMPASSIONATE				
			SLOAN, M CA-SOLID; COMPASSIONATE				
			STINE, ANTHONY CA-SOLID; COMPASSIONATE				
L	Jun-30-87		ANNUAL REPORT	87-16	DJF		870962
		(a)	PROGRESS RPT 86 INV.TREATED 3-76 & 89 TREATED 3-77 SINCE LST RPT.5/31/86				
L	Jul-29-87		CORRESPONDENCE FDA AUTH X-REF FOR MARKMAN TO STDY INTRAPERITONEAL	87-15	DJF		870963

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
16,332	IND		MITOXANTRONE CL 232,315 ANTICANCER AGENT				
L	Aug-03-87		CORRESPONDENCE DR. JD BITRAN CROSS REF OUR IND/REFRAC METATAST BREAST CA	87-19	DJF		871010
L	Aug-05-87		AMENDMENT INV / COMP USE	87-20	DJF		871011
		(a)	INVESTGTR DOCUMENTN at LEDERLE/003-076-0 INV LIST/COMP USE/JUNE & JULY/#'S 178-185 BORROW, SAMUEL CA-SOLID; COMPASSIONATE EISENBERG, PETER D CA-SOLID; COMPASSIONATE GLOWALLA, MICHAEL CA-SOLID; COMPASSIONATE KAMPEL, LEWIS CA-SOLID; COMPASSIONATE SALTZMAN, MARK CA-SOLID; COMPASSIONATE SPITZER, GARY CA-SOLID; COMPASSIONATE TIRUMALI, NAGENDRA CA-SOLID; COMPASSIONATE YAMAMOTO, KENNETH S CA-SOLID; COMPASSIONATE				
L	Aug-07-87		AMENDMENT PROT AMENDMENT #1 / #3-82	87-21	DJF		871004
		(a)	PROTOCOL AMENDMENT /003-082-0 PROT #3-82 AMEND OUTLINES DOSE ESCALATION FOR NEW PATIENTS				
L	Aug-12-87		AMENDMENT PI-M.MARKMAN TREATING 2ND PT/OVARIAN CA/1ST PT 5/29/87	87-22	DJF		871009

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA		NOVANTRONE *MITOXANTRONE INJ				
L	May-09-84		MEETING REQUEST MTG 5/22: POSSIBILITY OF MULTIPLE-DOSE CLASSIFICATION		GRP		831426
L	May-18-84		INITIAL SUBMISSION 166 VOLUMES. BREAST INDICATION (a) TABLE OF CONTENTS vols 1.1 - 1.26; OPTIONAL EXPANDED SUMMARY (b) LABEL # /PT 4 vol 1.26 (c) COMPONENTS & COMPOSITION # /PT 6,7 vol 1.26 (d) MANUF & CONTROLS vol 1.27-8 (e) PRECLINICAL # /PT 10 vols 1.29 - 1.39; RPT Nos. 1-159 (f) BIOPHARMACEUTIC PKG vols 1.40-44 (g) BIBLIOGRAPHY vols 1.45-48 (h) DRUG EXPER RPT vols 1.49-50 (i) CLINICAL STUDIES vols 1.51-2; PHARMACOKINETIC STUDIES (j) CLINICAL STUDIES vols 1.53-77; DOSE TOLERANCE STUDIES (k) CLINICAL STUDIES vol 1.78 - 1.150; CONTROLLED STUDIES (l) CLINICAL STUDIES vols 1.151-155; OTHER CLINICAL STUDIES (m) CLINICAL STUDIES vol 1.156; CLINICAL LAB STUDIES RELATED TO SAFETY (n) CLINICAL STUDIES vols 1.157 - 1.166; SPECIAL PATIENTS		DRS		831482
L	Oct-24-84		CORRESPONDENCE PATENT & EXCLUSIVITY INFO PER McGINNIS' REQUEST, 10/23/84		ECM		831985
L	Nov-12-84	L Oct-24-84	CORRESPONDENCE PATENT & EXCLUSIVITY INFO (CORRECTS 10/24/84 COMMUNICATION)		GWM		832039

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
L	Nov-28-84		CORRESPONDENCE	84-66	DJF		832068
			(a) SUMMARY, CLINICAL PROPOSED DRAFT SUMMARY BASIS OF APPROVAL				
L	Jan-23-85		CORRESPONDENCE AS REQUESTED BY CSO ALETA SINDELAR		DJF		850044
			(a) PUBLISHED RPTS METASTATIC BREAST CANCER (CANCER CLIN TRIALS 4:355-362, '81)				
L	Apr-17-85		MEETING AGENDA FOR 5/2/85 MTG re RESUBMN OF CLIN DATA FOR META BR CA		DJF		850327
L	May-28-85	M May-02-85	CORRESPONDENCE REVIEW OF LED's UNDERSTANDING OF THE 3/28 & 5/2/85 MEETINGS		DJF		850508
L	Jul-12-85	L May-18-84	NOT APPROVABLE LED MUST SUBMIT AMENDMENT CORRECTING DEFICIENCIES		DJF		850714
L	Oct-21-85	F Jul-12-85	AMENDMENT RESUBMISSION FOR BREAST INDICATION (INIT'L SUBM 5/18/84)		DJF		851114
F	Nov-20-85	L Oct-21-85	CORRESPONDENCE 10/21/85 SUBM CONSIDERED MAJOR AMNDMT -NEW 180 DAY REVIEW PD		DJF		851157
L	Nov-20-85	F Jul-12-85	AMENDMENT RESPONSE TO 7/12 DEFIC LTR re MANUF/CTRLS NOT ADDRESSD 10/18		DJF		860081
			(a) LABEL-REVISED DRAFT,CONTAINER # 17312 TEXT CODE: PRD2 10ml VIAL				
			(b) LABEL-REVISED DRAFT,BOX # 17311 TEXT CODE: PRD2 10ml VIAL				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA		NOVANTRONE *MITOXANTRONE INJ				
			(c) LABEL-REVISED DRAFT,CONTAINER # 17313 TEXT CODE: PRD2 15ml VIAL				
			(d) LABEL-REVISED DRAFT,BOX # 17314 TEXT CODE: PRD2 15ml VIAL				
			(e) LABEL-REVISED DRAFT,BOX # 17310 TEXT CODE: PRD2 12.5ml VIAL				
			(f) LABEL-REVISED DRAFT,BOX # 17309 TEXT CODE: PRD2 12.5ml VIAL				
			(g) LABEL-REVISED DRAFT,PKG INSERT # 17303 TEXT CODE: PRD4				
			(h) FORMULATION # /PT 7 COMPOSITION OF BOTH CLIN FORM'Ns I & II (PROP'd COMM'l FORM)				
			(i) CONTROLS # /PT 8(c) IN-PROCESS CTRLS--GOSPORT PRODUCTION (PER ITEM#2, 7/12 LTR)				
			(j) MONOGRAPH # /PT 8(d) SPECS FOR RAW MATERIAL & COMPONENTS				
			(k) AUTHORIZATION # /PT 8(n) HALDANE & WICKHAM LABS LTRS AUTH'g FDA TO X-REF THEIR DMFs				
			(l) STABILITY # /PT 8(p) SUMMARY & REPORTS				
			(m) ANALYSES REPORT OF ANALYTICAL FINDINGS FOR CL 232,315				
L	Dec-06-85	L Oct-21-85	CORRESPONDENCE REPL PAGES (REPRESENTING CORRECTIONS) 75-77, 87, 89	v2.41	DJF		851175 pp
L	Jan-10-86		AMENDMENT		GRP		860021
			(a) MANUF & CONTROLS HEINRICH MACK NACHF. AMNDMT TO DMF#5203 FOR MANUFg MITO BULK				
L	Jan-20-86	L Oct-21-85	CORRESPONDENCE		DJF		860032
			(a) CLINICAL STUDIES REANALYSIS OF DURATION OF RESPONSE DATA (NO SIGNIFICNT DIFF)				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA		NOVANTRONE *MITOXANTRONE INJ				
L	Jan-23-86		CORRESPONDENCE LIST OF INDIVIDUALS PARTICIPATING IN 3/6/86 ONCOL ADVIS MTNG		DJF		860066
L	Jan-23-86		CORRESPONDENCE		DJF		860068
			(a) SUMMARY, CLINICAL 20 COPIES FOR ADVISORY COMM REVIEW/MTG 3/6; NOT FILED IN NDA				
F	Jan-27-86	L Nov-20-85	CORRESPONDENCE 11/20/85 AMNDMT DEEMED "MAJOR" --ADDL 2mo ADDED TO REVIEW PD		DJF		860074
L	Jan-28-86		CORRESPONDENCE		DJF		860067
			(a) CASE REPORT FORM LISTING OF CRF's (AS REQ'd BY TURNER) FROM 10/18/85 SUBM				
L	Feb-05-86		TELEPHONE CALL MR. MEYER re FEASABILITY OF CYAN SPONSRSHP OF ADVIS COMM MTG		ECM		870059
F	Feb-18-86	L Jan-10-86	CORRESPONDENCE 1/10/86 AMNDMT DEEMED "MAJOR" --REVIEW PD EXT 1 Mo.--7/23/86		GRP		860127
L	Feb-25-86	L Oct-21-85	CORRESPONDENCE		DJF		860146
			(a) SAFETY UPDATE - CLINICAL SAFETY UPDATE OF 10/21/85 RESUBMISSION				
L	Feb-26-86	T Feb-13-86	CORRESPONDENCE RESPONSE TO BURKE'S ?? re CARDIOTOX RPT - v2.40, 10/21 RESUB		DJF		860152
E	Mar-14-86		MEETING ADV COMM MTG (9-2 FAVOR NOVANT "ALTERNATIVE" TO ADRIA IN MBC		ECM		870060

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
L	Mar-19-86	M Mar-14-86	CORRESPONDENCE GLOSSIES OF SLIDES USED IN LED PRES'n AT ADVIS COMMITTEE MTG		DJF		860226
L	Mar-24-86	M Mar-14-86	CORRESPONDENCE MEMO TO SUTHERLAND: FOLLOW-UP REMARKS OF MTG(APPRVL TIMETBL)		ECM		870061
F	May-30-86	L May-18-84	NOT APPROVABLE MANUFg, STABILITY, LABELING, CLINICAL PHARM, PK DEFICIENCIES		DJF		860528
L	Jun-09-86	F May-30-86	AMENDMENT RESPONSE TO MANUF'g & CONTROL DEFICIENCIES NOTED IN 5/30 LTR (a) MANUF & CONTROLS # 15201f(g) /PT 8h (b) FORMULA & SOI # /PT 8b (c) STABILITY REPORT # 86-494 /PT 8n 2mg/ml, UPDATE RPT		GRP	F	860538
L	Jun-10-86	F May-30-86	CORRESPONDENCE AS REQ'd, 4 COPIES OF METHODS VALIDATION PACKAGE		GRP		860537
L	Jul-16-86	F May-30-86	CORRESPONDENCE (a) LABEL # 14545 TEXT CODE: PRD5 INSERT PROPOSED BY FDA w/ LEDERLE ALTERNATIVE WORDg/DELET'Ns		DJF		860669
L	Aug-04-86		VALIDATION AS PER FDA CHEMIST (DR TOLGYESI) INSTRUCTIONS		GRP		860719

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
			(a) SAMPLES 1x5gm SAMPLES (CGBL & WG) & REFERENCE STNDS FOR VALIDATIONS				
L	Aug-06-86		VALIDATION SAMPLES/REFERENCES STNDS TO BE USED FOR VALIDATION STUDIES		GRP		860756
F	Aug-19-86	L Jul-16-86	CORRESPONDENCE 7/16/86 AMNDMT DEEMED "MAJOR"; ADDL 60 DAYS FOR REVIEW PD		GRP		860704
F	Sep-08-86	L Jun-10-86	CORRESPONDENCE JUNE 9&10 AMDMTS "MAJOR" --2mo ADDED TO REVIEW PD: 8/10/86		DJF		860827
F	Oct-07-86		NOT APPROVABLE		DJF		861059
L	Oct-17-86		MEETING LED REQUESTS MTG re FURTHER REQRMNTS FOR NDA APPROVAL		DJF		861033
L	Nov-24-86	M Dec-18-86	MEETING PROPOSED AGENDA & LIST OF LED ATTENDEES FOR 12/18/86 MEETING		DJF		870718
L	Dec-10-86	M Dec-18-86	MEETING BACKGROUND INFO FOR UPCOMING MTG, 12/18/86	86-40	DJF		870731
L	Mar-12-87	L Jun-23-27	AMENDMENT DATA TAPES W/FULL RPTS OF REFORMATTED SUMMARY TABLES		DJF		870982
L	Mar-12-87	L Dec-18-86	MEETING INTENT TO SUBMIT FULL RE-EVAL.& CLIN.SUMMARYOF 4-52		DJF		870981
			(a) CORRESPONDENCE INTENT TO SUBMT RE-EVAL. & CLIN SUMMARY OF STDY 4-52				

Led/ FDA	Event Date	Cross Ref Date		Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ						
L	Mar-19-87	F May-30-86		AMENDMENT 21 PRECLINICAL RPTS/9VOL INCLUDING FULL SUMMARIES FOR 3 STDS		DJF		870977
			(a)	PRECLINICAL REPORT(s) REQUEST FROM FDA-TEL 6/23 & 8/27				
F	Apr-23-87	Y Mar-12-87	*	TELEPHONE CALL DR G BURKE,MRO RE OUR 3/12/87 PROPOSAL FOR UPDATING 4-52, HE REQUESTED UPDATED SURVIVAL & CARDIOTOX DATA ALSO BE SUBMITTED FOR 3-48. THEY MIGHT ALSO BE INTERESTED IN SAME FOR 3-40. WILL CONFIRM IN OFFICIAL LETTER.		DJF	L	870291
F	Apr-27-87	L Mar-19-87		ACKNOWLEDGEMENT SUBM NOT SUFFICIENT-NOT BEING PROCESSED AS AMENDMENT		DJF		870976
L	May-05-87		#	TELEPHONE CALL DR G BURKE, MRO DR POSNER CALLED DR BURKE RE BREAST CANCER AMENDMENT AND PRE-NDA MTG ON LEUKEMIA. ALSO DISCUSSED THE POSSIBILITY OF A TREATMENT IND.		DJF		871452
F	May-08-87	Y Mar-12-87	#	TELEPHONE CALL DR KARL LINN, BIOMETRICS HE INDICATED HE WAS HAVING A PROBLEM READING THE CARCINOGENECITY TAPES(SUBMITTED ON 3/12/87) INTO HIS COMPUTER. DR GOLDBERG TO CALL HIM BACK ON THE MATTER.		DJF		870491
F	May-14-87		*	TELEPHONE CALL DR. CARL LINN, BIOSTAT 5/8/87-TAPES SUBM. 3/12/87 REQUESTED INFO RE CARCINOGENECITY TAPES PROVIDED TO FDA ON 3/12/87. DR GOLDBERG PROVIDED CLARIFICATION INCLUDING ADDITIONAL TAPE SPECS.		DJF		870502

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
L	May-15-87		CORRESPONDENCE INFO ON EFFECT OF NOV. IN LEUKEMIA IN PREP FOR PRE-NDA MEET		DJF		870636
L	May-21-87		# MEETING DR G BURKE, MRO OBTAINED ADVANCED COPY OF FDA LETTER REQUESTING ADDITIONAL DATA ON 3-40 & 3-48.		DJF		871336
F	May-28-87		* TELEPHONE CALL MS A SINDELAR,CSO PRE-NDA MTG TO DISCUSS LEUKEMIA FILING ARRANGED FOR JULY 7 AT 1:30PM IN 14B/45 AT FDA. DRS TEMPLE & BOTSTEIN + ONCOLOGY DIVISION STAFF WILL ATTEND.		DJF		870583
L	Jun-29-87		MEETING PREP FOR PRE-NDA MTG.7/7/87 - SENT TABLE OF CONTENTS	87-14	DJF		870969
			(a) CORRESPONDENCE SENT TABLE OF CONTENTS FOR LEUKEMIA FILING				
L	Jul-07-87		# MEETING DR. TEMPLE AND ONCOLOGY DIVISION MEMBERS		DJF		870789
L	Jul-21-87		CORRESPONDENCE MINUTES OF PRE-NDA MTG W/FDA 7/7/87		DJF		871322
L	Jul-21-87		* TELEPHONE CALL DR R TEMPLE,DIRECTOR DR CARTWRIGHT SPOKE WITH DR TEMPLE FOLLOWING UP OUR MTG OF 7/7/87. TEMPLE POSITIVE ABOUT THE LEUKEMIA CLAIM AND ANXIOUS TO RECEIVE DATA ON BREAST & LEUKEMIA ASAP AS YHE NEXT ADVISORY MTG IS SCHEDULED FOR EARLY DECEMBER.		DJF		871002

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
L	Jul-23-87		MEETING DR D HERSEY, SEC ONCOL ADV COMMITTEE NEXT ADVISORY COMMITTEE TENTATIVELY SCHEDULED FOR DECEMBER 7-8,1987.		DJF		870911
L	Jul-28-87		DRUG EXPERIENCE RPT SAFETY EVENT REPORT-NETHERLANDS #3062	87-17	DJF		870961
		(a)	SAFETY UPDATE DEAF & BLIND AFTER TREAMNT-DIED FEW DAYS LATER PAT.#3062				
L	Jul-29-87		CORRESPONDENCE LETTER OF AUTHORIZATION FOR SPEITZER	87-18	DJF		870960
		(a)	AUTHORIZATION STDYING ETOPOSIDE&THIO.W/AUTOLOGOUS MARROW SUPPT/BREST CANCR				
L	Aug-17-87	*	AMENDMENT RAW DATA FOR UPDATES ON 4-52, 3-40, & 3-48		DJF		871091
		(a)	CASE REPORT FORM FDA REQUESTS:5/30/86;10/6/86;5/10,1987:PROT 4-52,3-40,3-48 RAW DATA SUBMITTED FOR BREAST STUDIES 4-52, 3-40, & 3-48				
L	Aug-26-87		TELEPHONE CALL DR D HERSEY, SEC ONCOL DRUGS ADV COMM LATEST LIST OF PANEL MEMBERS FROM ADVISORY PANEL REC'D.MTG TENTATIVELY SCHEDULED FOR 12/7&8.		DJF		871335
L	Sep-09-87		CORRESPONDENCE RE-REQUEST FOR GOSPORT INSPECTION AFTER 1ST REQ. CANCELLED		GRP		871391
L	Sep-11-87	*	TELEPHONE CALL DR J JOHNSON, GR DIRECTOR ONCOLOGY		DJF		871111

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
			DR JOHNSON RECEPTIVE TO PIECEMEAL SUBMISSION OF LEUKEMIA CLAIM. WOULD DO HIS BEST TO REVIEW BEFORE ADVISORY MTG IN DECEMBER.				
F	Sep-15-87		* TELEPHONE CALL DR G BURKE, MRO		DJF		871117
			REQUESTED CRFS FOR 4-52 RESPONDERS WHOSE RAW DATA WERE NOT INCLUDED IN 8/87 FILING.				
L	Sep-16-87		* TELEPHONE CALL DR J JOHNSON, ONCOLOGY GROUP DIRECTOR		DJF		871128
			DISCUSSED SCHEDULE FOR PIECEMEAL FILING OF LEUKEMIA CLAIM & CONTENT OF PACKAGE FOR ADVISORY COMMITTEE IN DECEMBER.				
L	Sep-16-87		CORRESPONDENCE LIST OF SUBMISSIONS FOR NEXT MONTH FOR BREAST & LEUKEMIA		DJF		871230
L	Sep-16-87		CORRESPONDENCE LIST OF RESPONDERS IN THE 4-52 STUDY OF NOV. IN BREAST CANCER		DJF		871229
			(a) CORRESPONDENCE LIST OF RESPONDERS IN 4-52 STUDY OF NOV. IN BREAST CANCER.				
L	Sep-18-87	L Sep-11-87	TELEPHONE CALL		DJF		871199
			NOTIFIED DR.JOHNSON ABOUT PIECEMEAL SUBM. OF COMP FOR LEUKEMIA & BREAST WHICH WILL HOPEFULLY ALLOW INCLUSION OF BOTH CLAIMS ON AGENDA FOR ADV. COMM MTG.				
L	Sep-21-87		* AMENDMENT CASE RECORDS FOR 3-74 & 3-603 LEUKEMIA TRIALS		DJF		871228
			(a) CLINICAL STUDIES TRETMNT OF ADLT ACUTE NON-LYMPH LEUKEMIA/OD GRANTED 7/13/87				

Led/ FDA	Event Date	Cross Ref Date		Description	Amendment/ Supplement	Contact	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ						
				CRF'S FOR 3-74 AND 3-603 FILED TO FDA AS PART OF APRECLINICAL SUBMISSION FOR A CLAIM IN ANLL. ADDITIONAL SUBMISSIONS PROJECTED FOR SEPTEMBER 30 AND OCTOBER 15.				
L	Sep-22-87			TELEPHONE CALL DR D HERSEY, SEC ONCOL DRUGS ADV COM		DJF		871130
				DR ALBERT BERNARTH ADDED TO ONCOLOGIC DRUGS ADVISORY PANEL. NO OFFICIAL AGENDA ITEMS IDENTIFIED.				
L	Sep-30-87	F	*	AMENDMENT 5/30/86,10/7/86, 5/20/87,MTGS: 12/18/86 & 7/7/87		DJF		871198
			(a)	CORRESPONDENCE RESPONSE TO PHARMACOK.QUESTIONS FROM FDA LETTER 5/30/86				
			(b)	SUMMARY, CLINICAL UPDATED 4-52 SUMM./SURV.CURVES 3-40&3-48/CLIN.PHARM.SUMM.				
				UPDATE OF 4-52,3-40 AND 3-48 + RESPONSE TO PK QUESTIONS-REPRESENTS A FULL RESPONSE TO FDA LETTERS 5/30/86, 10/7/86 AND 5/20/87.				
L	Oct-01-87		*	CORRESPONDENCE DR CARTWRIGHT'S COMMENTS TO DR TEMPLE RE BR & LEUK SUBMISS.		DJF		871161
				DR CARTWRIGHT INFORMS DR TEMPLE VIA LETTER ABOUT OUR PLANS FOR PIECEMEAL FILINGS FOR THE BREAST AND LEUKEMIA CLAIMS.				
L	Oct-02-87		*	AMENDMENT CLINICAL DATA TO SUPP. ADULT ACUTE NON-LYMPHOCYTIC LEUKEMIA		DJF		871197
			(a)	CLINICAL REPORT(s) # /PT b MULTI-CTR STDY 3-74+ARA-CVS.CERUBIDINE+ARA-C/11 SUPP.STUDIES				
			(b)	BIBLIOGRAPHY +REPRINTS ITEM#8 REPRES.COMBINED CLIN & STAT PRESENTATION				

Led/ FDA	Event Date	Cross Ref Date		Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ						
				NDA AMENDMENT INCLUDING CLINICAL REPORTS OF 3-74 & 11 SUPPORTIVE TRIALS + A CLINICAL BIB SUBMITTED TO FDA.				
L	Oct-09-87		#	TELEPHONE CALL		DJF		871196
				OCT 8 SPOKE W/DR. HERSEY ABOUT PREP FOR ADVISORY COMM. IN DEC. HE NOTED BOTH LEUK. & BREAST CLAIMS FOR NOV. WERE TENTATIVELY ON AGENDA. LEUK-MORNING OF DEC.7 W/ BREAST IN AFTERNOON. CONTINGENT UPON FDA REVIEWING PKGS. SUBM. & ONES TO BE FILED.HE ADDED THAT CRITERIA FOR APPROV. OF A SOLID TUMOR TYPE (OVARIAN CANCER) MIGHT BE AN AGENDA ITEM.NEEDTO C/B IN A COUPLE WEEKS FOR MORE INFO.				
F	Oct-16-87			VALIDATION VALIDATION TESTING COMPLETE & SUITABLE W/MODIFICATIONS		GRP		880066
F	Oct-16-87		#	VALIDATION METHODS VALIDATION APPROVED WITH SOME MODIFICATIONS		GRP		880036
F	Oct-16-87		#	TELEPHONE CALL DR G BURKE, MRO		DJF		871265
				SPOKE WITH DR MARCUS RE CASES OF HYPERBILIRUBINEMIA IN 3-74 LEUKEMIC PATIENTS AND CODING/TRANSCRIPTION ERRORS IN DOCUMENTING ADR'S.				
L	Oct-19-87		*	CORRESPONDENCE PROPOSED LABELNG-REQUESTED BY A.SINDELAR 10/16/87-BREAST		DJF		871321
				PROPOSED BREAST LABELING FORWARDED TO FDA.				
F	Oct-20-87			ACKNOWLEDGEMENT BR CA DEFICIENCIES:ITEMS 6 (PHARMACO) & 8 (CLIN & STAT)		DJF		871418

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
19-297 NDA NOVANTRONE *MITOXANTRONE INJ							
L	Oct-21-87	L Mar-12-87	CORRESPONDENCE REPLCMNT TAPE-NB8238 RAT CARCINOGEN. STDY #81152		DJF		871320
L	Oct-22-87		* CORRESPONDENCE DOCUMENTATION FOR ADVISORY COMM FOR DECEMBER MTG		DJF		871319
			(a) LABEL-DRAFT,PACKAGE INSERT COVERNG USE IN BOTH LEUKEMIA & BREAST CANCER (b) CLINICAL REPORT(s) MULTICENTER STUDIES: 3-603,NOV + ARA-C VS CERUBIDINE+ARA-C FINAL INSTALLMENT OF CLINICAL DATA TO SUPPORT THE LEUKEMIA(ANLL) CLAIM FILED AT FDA. SUBMISSION INCLUDES 3-603 CLINICAL REPORT, INTEGRATED SUMMARIES OF SAFETY & EFFICACY AND PROPOSED LABELING COVERING BOTH THE LEUKEMIA & BREAST CA CLAIMS.				
F	Oct-28-87		* TELEPHONE CALL DR G BURKE, MRO PHONED DR S MARCUS REQUESTING INFORMATION ON LEUKEMIA STUDY 3-603 RELATED TO MISSING BONE MARROW DATA & PROBLEMS IN THE PACIFIC REGION.		DJF		871328
F	Oct-29-87		# TELEPHONE CALL DR R STEIN, FDA BIOSTATISTICIAN PHONED DR J GOLDBERG RE QUESTIONS ON THE 4-52 BREAST CA REPORT RELATED TO 80 CUTOFF VALUE FOR SGOT & ESTIMATION OF TTD.		DJF		871348
F	Oct-30-87		* TELEPHONE CALL DR G BURKE, MRO CALLED DR S MARCUS RE HIS RECENT REQUEST FOR THE MISSING BONE MARROW RATING DATA.		DJF		871337
L	Nov-02-87		# RESPONSE TO FDA REPLAC OF APP VI TO 3-603 STUDY REQ BY DR BURKE 10/28/87		DJF		871445

Led/ FDA	Event Date	Cross Ref Date		Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ						
				REPLACEMENT OF APP VI OF THE 3-603 STUDY SUBMITTED ON 10/22/87 FILED PER DR BURKE'S REQUEST OF 10/28/87				
L	Nov-04-87			CORRESPONDENCE HANDOUTS FOR 12/7-8/87 ONCOLOG ADV COMM MTG (20 CC)		DJF		871413
L	Nov-06-87			CORRESPONDENCE REPLACEMENT COPY:APPEND#6 SUB.11/2/87;APPEND#14 SUB.10/22/87		DJF		871417
F	Nov-06-87		#	TELEPHONE CALL DR D HERSEY, SEC ONCOL DRUGS ADV COMM		DJF		871376
				QUESTIONS FROM ONCOLOGY DIV TO ADVISORY PANEL OBTAINED.				
L	Nov-12-87			PERIODIC REPORT 10/1/86 - 9/30/87		AH		880091
L	Nov-12-87		#	RESPONSE TO FDA LISTING OF LAB CONVERSION FACTORS FILED		DJF		871446
				A LISTING OF LAB CONVERSION FACTORS FOR THE 3-603 STUDY FILED PER DR BURKE'S REQUEST.				
F	Nov-13-87		*	TELEPHONE CALL DR G BURKE, MRO		DJF		871395
				REQUESTED ADD'L ANALYSES OF SURVIVAL,RR & RESPONSE DURATION FOR INTENT-TO-TREAT PTS(EXCEPT THOSE WRONGLY DIAGNOSED) IN 3-74 & 3-603. ALSO TO RUN SAME DELETING HONG KONG & TAIWAN.				
L	Nov-19-87		#	TELEPHONE CALL DR G BURKE, MRO		DJF		871431

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
			DR S MARCUS PHONED RE ERRATA IN THE 3-603 LEUKEMIA STUDY.				
F	Nov-19-87		# TELEPHONE CALL DR R STEIN, BIOSTATISTICIAN		DJF		871451
			REQUESTED FROM MR WEISS CALCULATION OF CONFIDENCE LIMITS FROM THE LEUKEMIA STUDIES 3-74 & 3-603.				
F	Nov-24-87		# TELEPHONE CALL DR G TURNER, OFFICE OF SCIENTIFIC INVEST		DJF		871439
			REQUESTED 3 VOLUMESFROM 10/2/87 LEUKEMIA SUBMISSION CONTAINING CLINICAL REPORT OF 3-74 STUDY TO AID IN HIS SELECTION OF SITES TO AUDIT				
L	Nov-24-87		# CORRESPONDENCE 3-40(BREAST) SUBGROUP ANALYS BASED ON PROG FACTORS		DJF		871448
			AN ANALYSIS OF SURVIVAL DATA FROM THE 3-40 BREAST STUDY WAS SUBMITTED FOR SUBGROUPS BASED ON PROGNOSTIC FACTORS(AS WAS DONE FOR YHE 4-52 STUDY).				
L	Nov-24-87		# RESPONSE TO FDA ADD'N SUBSET ANALYS 3-74/3-603 & EVAL OF SUPP CARE 3-603		DJF		871447
			ADD'N SUBSET ANALYSES FOR RESPONSE RATE, SURVIVAL, & RESPONSE DURATION FILED PER DR BURKE,S REQUEST. ALSO AN EVALUATION OF THE QUALITY OF SUPPORTIVE CARE FOR PATIENTS WITH INFECTIONS IN 3-603 WAS PROVIDED.				
F	Nov-25-87		# TELEPHONE CALL DR G BURKE, MRO & DR J JOHNSON, GR DIR ONCOL		DJF		871437
			ASKED THAT WE RESTRICT OUR PRESENTATIONS ON LEUKEMIA & BREAST CANCER TO 45 MIN EACH.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact -------	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
L	Nov-30-87		RESPONSE TO FDA COPIES OF 3-74 VOLS(LEUK) TO DR G TURNER AS REQUESTED		DJF		871440
		(a)	CORRESPONDENCE FDA REQ FOR VOL 1,2,3(14.1,14.2,14.3)LEUKEMIA 3-74 STUDY				
L	Nov-30-87		# TELEPHONE CALL DR G BURKE, MRO		DJF		871449
			REQUESTED SUPPORTIVE CARE INFO ON PATIENTS WHO DIED DURING CONSOLIDATION THERAPY IN THE 3-74 & 3-603 LEUKEMIA STUDIES. ALSO WANTED HAZARD RATIOS FOR THE 3-603 SUBSET ANALYSES PROVIDED 11/24/87. ASKED THAT WE OFFICIALLY SUBMIT THE BREAST CA SUMMARY SENT TO THE ADVISORY PANEL TO THE NDA.				
L	Dec-01-87		CORRESPONDENCE LIST OF LEDERLE PRESENTERS(NOVANTRONE)@ FDA ADV COMM MTG		DJF		871490
L	Dec-01-87		# TELEPHONE CALL DR D HERSEY, SEC ONCOL DRUGS ADV COMM		DJF		871453
			DR DEAN BRENNER OF ROSWELL PARK WILL BE THE NEWEST MEMBER OF THE ADVISORY PANEL.				
L	Dec-02-87		# TELEPHONE CALL DR G BURKE, MRO		DJF		871454
			DR S MARCUS CALLED ABOUT THE PRESENTATION OF SUPPORTIVE CARE DATA FOR PATIENTS IN THE 3-603 LEUKEMIA STUDY.				
L	Dec-03-87		# TELEPHONE CALL DR G BURKE, MRO		DJF		871462
			PROVIDED DR BURKE WITH SURVIVAL HAZARD RATIOS ON SUBGROUPS OF PATIENTS FROM THE 3-603 LEUKEMIA STUDY REQUESTED ON 11/30/87.				

Led/ FDA	Event Date	Cross Ref Date	Description	Amendment/ Supplement	Contact	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ					
L	Dec-07-87		* MEETING ONCOLOGIC DRUGS ADVISORY COMM MTG LEUKEMIA APPROVED ONCOLOGIC DRUGS ADVISORY COMMITTEE MEETING - NOVANTRONE APPROVED 7-2(2 ABSTAINING) FOR FIRST-LINE USE IN COMBO VS ANLL. 11-0 VOTE AGAINST ITS USE AS SINGLE USE IN RELAPSED ANLL. USE IN BREAST CANCER NOT APPROVED BY AN 8-3 VOTE.		DJF		871524
F	Dec-08-87		# MEETING DR G TURNER, OFFICE OF SCIENTIFIC INVESTIGATION		DJF		871508
L	Dec-09-87		* RESPONSE TO FDA		DJF		871520
			(a) CASE REPORT FORM /003-074-0 RANDOM CRFs FROM #3-74 REQ BY DR G TURNER(FDA)FOR AUDITING				
F	Dec-09-87		# TELEPHONE CALL DR G BURKE, MRO CALLED DR MARCUS RE WORDING OF THE PI RELATED TO THE CONSOLIDATION PHASE OF TREATMENT AND LISTING OF ADRS FOR THE INDUCTION PHASE IN STUDY 3-74.		DJF		871527
L	Dec-10-87	F Oct-15-87	RESPONSE TO FDA WE AGREE TO REQUESTED MODIFICATIONS TO ANALYTICAL TESTING		GRP		880030
L	Dec-10-87		* RESPONSE TO FDA DRAFT LABELING FOR USE IN LEUKEMIA		DJF		871521
			(a) LABEL,DRAFT,PACKAGE INSERT PROP.DRAFTLABEL FOR ANLL + ADV REAC LIST(3=74/3-603)DR.BURKE DRAFT LABELING FOR USE IN ANLL REFLECTING SEVERAL CONVERSATIONS WITH DR G BURKE WERE SUBMITTED TO FDA ALONG WITH A WANG DISKETTE.				

Led/ FDA	Event Date	Cross Ref Date		Description	Amendment/ Supplement	Contact	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ						
L	Dec-10-87	F Oct-16-87	#	CORRESPONDENCE WE AGREE TO SUGGESTED ANALYTICAL MODIFICATIONS		GRP		880013
F	Dec-11-87		#	TELEPHONE CALL DR G BURKE, MRO CALLED DRS MARCUS AND FOLEY SEVERAL TIMES RE THE FINAL LABELING FOR USE IN ANLL. FDA HAS MADE A NUMBER OF REVISIONS TO OUR PROPSED TEXT SUBMITTED EARLIER IN THE DAY EG THE PK SECTION AND THAT DEALING WITH CARDIOTOXICITY.		DJF		871528
F	Dec-14-87		*	MEETING DR G BURKE, MRO & MS A SINDELAR,CSO DRS CARTWRIGHT & SALETAN WERE ASKED TO STOP OFF AT THE ONCOLOGY DIV TO DISCUSS REVISIONS TO OUR PROPOSED PI SUBMITTED ON 12/11/87. AGREEMENT WAS REACHED ON REVISIONS.		DJF		871539
F	Dec-15-87		*	TELEPHONE CALL MS A SINDELAR, CSO CALLED TO INDICATE TWO ADDITIONAL CHANGES TO PI RE SINGLE DOSE USE AND CHANGE OF LABEL FROM "FOR INJECTION" TO "INJECTION". WE EXPESSED OUR OBJECTIONS TO THE LATTER REVISION FROM A SAFETY VIEWPOINT.		DJF		871540
F	Dec-23-87		*	APPROVAL APPROVAL FOR INITIAL RX OF ANLL IN COMBINATION		DJF		880009
L	Dec-30-87		#	TELEPHONE CALL MR K FEATHER, DIR DIV DRUG ADVERTISING APPRROVED TRADEMARK NOVANTRONE MITOXANTRONE HCL FOR PRE-LAUNCH REMINDER AD.		NAS		880007

Led/ FDA	Event Date	Cross Ref Date		Description	Amendment/ Supplement	Contact	Resp Due	Event ID
19-297	NDA	NOVANTRONE *MITOXANTRONE INJ						
L	Jan-04-88		#	TELEPHONE CALL MS A SINDELAR, CSO REVISED ADR TABLE AGREED TO FOR FINAL PRINTED LABELING.		DJF		880008
F	Jan-12-88	L Jan-05-88	*	ACKNOWLEDGEMENT FDA ACKNOWLEDGES RECEIPT OF SUPP S001-RCPT DATE 1/12/88	S001	GRP		880132
L	Jan-20-88	L Dec-20-87	*	SUPPLEMENT SUBMISSION OF PRESERVATIVE EFFICACY FOR MULTIPLE DOSE VIAL		GRP		880135

EXHIBIT D

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

U.S. Patent No. 4278689
Issued July 14, 1981

Inventors: Keith C. Murdock
Frederick E. Durr

Assignee: AMERICAN CYANAMID COMPANY, One Cyanamid Plaza, Wayne, New Jersey 07470

Title: 1,4-Bis(Substituted-Amino)-5,8-Dihydroxy-anthraquinones and Leuco Bases Thereof

Commissioner of Patents
and Trademarks
Washington, D.C. 20231

SIR:

DECLARATION IN SUPPORT OF APPLICATION FOR EXTENSION OF TERM OF U.S. PATENT NO.4278689

Alphonse R. Noë hereby declares that he is the Manager of the Patent Law Department of the AMERICAN CYANAMID COMPANY; and further declares:

THAT by a resolution of the Board of Directors of the AMERICAN CYANAMID COMPANY (a copy of which is attached hereto and made a part of this declaration), he is authorized to execute and file with the United States Patent and Trademark Office such documents as he may deem to be necessary from time to time;

THAT this declaration is in support of and filed with the accompanying application for extension of the term of U.S. Patent No. 4278689;

THAT the AMERICAN CYANAMID COMPANY is the assignee of record of U.S. Patent No. 4278689 by an

assignment recorded at frame 214 of reel 3507 in the United States Patent and Trademark Office;

THAT he has reviewed and understands the contents of the accompanying application being submitted pursuant to section D of the GUIDELINES FOR EXTENSION OF PATENT TERM UNDER 35 U.S.C. 156 as published in 1047 OG 16-20 (1984);

THAT he verily believes U.S. Patent No. 4278689 is subject to extension pursuant to section A of the hereinabove-identified GUIDELINES;

THAT he verily believes an extension of the length claimed in the accompanying application is fully justified under 35 U.S.C. 156;

THAT he verily believes U.S. Patent No. 4278689 for which the extension is being sought meets the conditions for extension of the term of a patent as set forth in section B of the hereinabove-identified GUIDELINES; and

THAT all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Alphonse R. Noë
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Stamford, CT 06904-0060
(203)348-7331

EAC/jhr
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CERTIFICATE

I, D. C. Droste, Assistant Secretary of American Cyanamid Company, a Maine corporation (the Company), hereby certify that the following is a complete and accurate copy of a resolution duly adopted by the Board of Directors of the Company at a regular meeting held on October 17, 1972, at which meeting a quorum was present and acting throughout, and that the same has not been rescinded or further amended and is now in full force and effect:

> RESOLVED: That any one of the Chairman of the Board, the President, the Vice Presidents, the Treasurer, the Assistant Treasurers, the Secretary, the Assistant Secretaries, the Manager of the Patent Law Department, and the Manager of the Trademark Copyright Law Department, be, and he hereby is, authorized, in the name and on behalf of this Company, to execute such powers of attorney and other documents, and to make such affidavits, as the person executing such documents or making such affidavits may deem to be necessary or desirable, from time to time, in connection with Letters Patent or trademark registrations, and applications for Letters Patent or trademark registrations, or in connection with any opposition, nullity, revocation, infringement or cancellation proceedings relating to Letters Patent or trademark registrations and to applications for Letters Patent or trademark registrations of other parties.

I FURTHER CERTIFY that A. R. Noe is Manager of the Patent Law Department of this Company.

IN WITNESS WHEREOF, I have hereunto set my hand and affixed the seal of this Company this 1st day of February, 1988.

Assistant Secretary